FIGURE 1A

```
   1  CGGATGCTGC TGCTACTGTC ACTTCTGCCG CTGCCGCTGT TGTTACAGAT
  51  TTTGCTTTTG CTCCTTCTAC CGCATGACAA TTGTTTTCCT CGCCTAAGCA
 101  GATACCAGCC TCAGATGCTC AAGGTGAGAG TCTTGCCTTT CGCTCTGGGC
 151  TATTGGTTCA CTTAATCCGG TCAATTTGTT CGCTGCTCGT GGTTGTCTTT
 201  CTCCCCGCCC TCCTTCCCCC TGTTTTGTTT TGTTTCGCTT GCTTTCGGGG
 251  GGACGCTCCT TCCCTCAGTC AGAAGAGCTG GAATTGCTTG AGAGGCGTAT
 301  AAGGAATTAT AAAAGTGGCC AGGAAACACG AGCGCAGTGA CTGCAGAGCT
 351  GCCCTTGGCT TCGGCAAGGC AGCGTGAGCG GCAGAGGGCT CGGGCAGGGG
 401  GCGGGGGGTC TCCTTTTTCC CGTGCGTTCC TCTTCTCCCA GTTCGGATGA
 451  TGTTGCTGTT TCGGACCTCT CGCTGACTCC TGCCCTGTGA TTTTTGCTGA
 501  GCGCTGTGAC TGTTACTCCG TCTCTTTCTG TCTGTGTTTC ACAGTAATGG
 551  ACTGTGATAG AGTTAAGGCC TTTTGGAGGT GAGCTGTGTC ACAGCTGATG
 601  CTTAAACATG TCTGAAGTAG GCACCGAGAC TTTCCCCAGC CCCTCGGCTC
 651  AGCTGAGCCC TGATGCATCC CTTGGCGGGC TCCCGGCTGA GGAGAACATG
 701  CCGGGGCCCC ACAGAGAGGA CAGCAGGGTC CCAGGTGTGG CAGGCCTGGC
 751  CTCGACCTGC TGCGTGTGCC TGGAAGCAGA GCGACTGAAG GGCTGCCTCA
 801  ACTCTGAGAA GATCTGCATC GCCCCTATCC TGGCTTGCCT GCTCAGCCTC
 851  TGCCTCTGCA TTGCTGGCCT CAAGTGGGTC TTTGTGGACA AGATTTTTGA
 901  GTATGACTCT CCTACACACC TTGACCCTGG GAGGATAGGA CAAGACCCAA
 951  GGAGCACTGT GGATCCTACA GCTCTGTCTG CCTGGGTGCC TTCGGAGGTG
1001  TATGCCTCAC CCTTCCCCAT ACCTAGCCTT GAGAGCAAGG CTGAAGTGAC
1051  AGTGCAAACT GACAGCTCGC TCGTGCCCTC CAGGCCCTTC CTTCAGCCTT
1101  CTCTCTACAA CCGCATCCTA GATGTCGGGT TGTGGTCCTC TGCCACACCG
1151  TCACTGTCAC CATCCTCCCT GGAGCCTACC ACGGCATCTC AGGCACAAGC
1201  AACAGAAACC AATCTCCAAA CTGCTCCAAA ACTTTCCACT TCTACATCTA
1251  CAACTGGGAC AAGTCATCTC ACAAAATGTG ACATAAAGCA GAAAGCCTTC
1301  TGTGTAAATG GGGGAGAGTG CTACATGGTT AAAGACCTCC CAAACCCTCC
```

FIGURE 1B

1351 ACGATACCTA TGCAGGTGCC CAAATGAATT TACTGGTGAT CGCTGCCAAA

1401 ACTACGTAAT GGCCAGCTTC TACAAGCATC TTGGGATTGA ATTTATGGAA

1451 GCTGAGGAAC TGTACCAGAA ACGGGTGCTG ACCATAACTG GCATTTGCAT

1501 TGCTCTTCTA GTAGTTGGCA TCATGTGTGT GGTGGCCTAC TGCAAAACCA

1551 AGAAGCAGAG GAAAAAGTTG CATGACCGCC TTCGGCAGAG CCTTCGCTCA

1601 GAGAGGAACA ACGTTATGAA CATGGCAAAT GGGCCACACC ACCCCAACCC

1651 ACCACCAGAC AATGTCCAGC TGGTGAATCA GTACGTTTCA AAAAACATAA

1701 TCTCCAGTGA ACGTGTCGTT GAGCGAGAAA CCGAGACCTC GTTTTCCACA

1751 AGCCACTACA CCTCAACAAC TCATCACTCC ATGAÇAGTCA CCCAGACGCC

1801 TAGCCACAGC TGGAGTAATG GCCATACCGA AAGCATTCTC TCCGAAAGCC

1851 ACTCCGTGCT CGTCAGCTCC TCAGTGGAGA ATAGCAGGCA CACCAGCCCA

1901 ACAGGGCCAC GAGGCCGCCT CAATGGCATT GGTGGGCCAA GGGAAGGCAA

1951 CAGCTTCCTC CGGCATGCAA GAGAGACCCC TGACTCCTAC CGAGACTCTC

2001 CTCACAGTGA AAGGTATGTC TCAGCTATGA CCACACCAGC TCGCATGTCA

2051 CCCGTTGATT TCCACACTCC AACTTCTCCC AAGTCCCCTC CATCTGAAAT

2101 GTCACCACCA GTTTCCAGCT TGACCATCTC CATCCCTTCG GTGGCGGTGA

2151 GTCCCTTTAT GGACGAGGAG AGACCGCTGC TGTTGGTGAC CCCACCACGG

2201 CTGCGTGAGA AGTACGACAA CCACCTTCAG CAATTCAACT CCTTCCACAA

2251 CAATCCCACC CATGAGAGCA ACAGTCTGCC ACCCAGTCCT CTGAGGATAG

2301 TGGAGGATGA AGAGTATGAG ACCACGCAGG AGTACGAACC AGCACAGGAG

2351 CCTCCAAAGA AACTCACCAA CAGCCGGAGG GTGAAAAGAA CAAAGCCCAA

2401 TGGCCATATT TCCAGCAGGG TAGAAGTGGA CTCCGACACA AGCTCTCAGA

2451 GCACTAGCTC TGAGAGCGAA ACAGAAGATG AAAGAATAGG TGAGGATACA

2501 CCATTTCTTA GCATACAAAA TCCCATGGCA ACCAGTCTGG AGCCAGCCGC

2551 TGCATATCGG CTGGCTGAGA ACAGGACTAA CCCGGCAAAT CGCTTCTCCA

2601 CACCAGAAGA GTTGCAAGCA AGGTTGTCCA GTGTAATAGC TAACCAAGAC

2651 CCTATTGCTG TATAAGACAT AAACAAAACA CATAGATTCA CATGTAAAAC

FIGURE 1C

2701 TTTATTTTAT ATAATGAAGT ATTCCACCTT TAAATTAAAC AATTTATTTT

2751 ATTTTAGCAA TTCCGCTGAT AGAAAACAAG AGTGGAAAAA GAAACTTTTA

2801 TAAATTAAGT ATACGTATGT ACAAATGTGT TATGTGCCAT ATGTAGCAAT

2851 TTTTTACAGT ATTTCCAAAA TGGGGAAAGA TATCAATGGT GCCTTTATGT

2901 TATGTTATGT TGAGAGCAAG TTTTGTACAG CTACAATGAT TGCTGTCCCG

2951 TAGTATTTTG CAAAACCTTC TAGCCCTCAG TTGTTCTGGC TTTTTTGTGC

3001 ATTGCATTAT AATGACTGGA TGTATGATTT GCAAGAATTG CAGAAGTCCC

3051 CATTTGCTTG TTGTGGAATC CCCAGATCAA AAAGCCCTGT TATGGCACTC

3101 ACACCCTATC CACTTCACCA GGAAAAAAAA AAAATCAAAA AAAAAAAAAA

3151 AAAAAAAAGA AAAGAAAGAG AAAAAAGAAA AGAAAAAGAA AAAAAAAGCT

3201 GAAAAAATAA AA

FIGURE 2

```
   1  GCCCYCHFCR CRCCYRFCFC SFYRMTIVFL A*ADTSLRCS R*ESCLSLWA
  51  IGSLNPVNLF AARGCLSPRP PSPCFVLFRL LSGGRSFPQS EELELLERRI
 101  RNYKSGQETR AQ*LQSCPWL RQGSVSGRGL GQGAGGLLFP VRSSSPSSDD
 151  VAVSDLSLTP AL*FLLSAVT VTPSLSVCVS Q*WTVIELRP FGGELCHS*C
 201  LNMSEVGTET FPSPSAQLSP DASLGGLPAE ENMPGPHRED SRVPGVAGLA
 251  STCCVCLEAE RLKGCLNSEK ICIAPILACL LSLCLCIAGL KWVFVDKIFE
 301  YDSPTHLDPG RIGQDPRSTV DPTALSAWVP SEVYASPFPI PSLESKAEVT
 351  VQTDSSLVPS RPFLQPSLYN RILDVGLWSS ATPSLSPSSL EPTTASQAQA
 401  TETNLQTAPK LSTSTSTTGT SHLTKCDIKQ KAFCVNGGEC YMVKDLPNPP
 451  RYLCRCPNEF TGDRCQNYVM ASFYKHLGIE FMEAEELYQK RVLTITGICI
 501  ALLVVGIMCV VAYCKTKKQR KKLHDRLRQS LRSERNNVMN MANGPHHPNP
 551  PPDNVQLVNQ YVSKNIISSE RVVERETETS FSTSHYTSTT HHSMTVTQTP
 601  SHSWSNGHTE SILSESHSVL VSSSVENSRH TSPTGPRGRL NGIGGPREGN
 651  SFLRHARETP DSYRDSPHSE RYVSAMTTPA RMSPVDFHTP TSPKSPPSEM
 701  SPPVSSLTIS IPSVAVSPFM DEERPLLLVT PPRLREKYDN HLQQFNSFHN
 751  NPTHESNSLP PSPLRIVEDE EYETTQEYEP AQEPPKKLTN SRRVKRTKPN
 801  GHISSRVEVD SDTSSQSTSS ESETEDERIG EDTPFLSIQN PMATSLEPAA
 851  AYRLAENRTN PANRFSTPEE LQARLSSVIA NQDPIAV*DI NKTHRFTCKT
 901  LFYIMKYSTF KLNNLFYFSN SADRKQEWKK KLL*IKYTYV QMCYVPYVAI
 951  FYSISKMGKD INGAFMLCYV ESKFCTATMI AVP*YFAKPS SPQLFWLFCA
1001  LHYNDWMYDL QELQKSPFAC CGIPRSKSPV MALTPYPLHQ EKKKIKKKKK
1051  KKRKEREKRK EKEKKS*KNK
```

FIGURE 3

```
   1  CGGCCTGTAA GATGCTGTAT CATTTGGTTG GGGGGGCCTC TGCGTGGTAA
  51  TGGACCGTGA GAGCGGCCAG GCCTTCTTCT GGAGGTGAGC CGATGGAGAT
 101  TTATTCCCCA GACATGTCTG AGGTCGCCGC CGAGAGGTCC TCCAGCCCCT
 151  CCACTCAGCT GAGTGCAGAC CCATCTCTTG ATGGGCTTCC GGCAGCAGAA
 201  GACATGCCAG AGCCCCAGAC TGAAGATGGG AGAACCCCTG GACTCGTGGG
 251  CCTGGCCGTG CCCTGCTGTG CGTGCCTAGA AGCTGAGCGC CTGAGAGGTT
 301  GCCTCAACTC AGAGAAAATC TGCATTGTCC CCATCCTGGC TTGCCTGGTC
 351  AGCCTCTGCC TCTGCATCGC CGGCCTCAAG TGGGTATTTG TGGACAAGAT
 401  CTTTGAATAT GACTCTCCTA CTCACCTTGA CCCTGGGGGG TTAGGCCAGG
 451  ACCCTATTAT TTCTCTGGAC GCAACTGCTG CCTCAGCTGT GTGGGTGTCG
 501  TCTGAGGCAT ACACTTCACC TGTCTCTAGG GCTCAATCTG AAAGTGAGGT
 551  TCAAGTTACA GTGCAAGGTG ACAAGGCTGT TGTCTCCTTT GAACCATCAG
 601  CGGCACCGAC ACCGAAGAAT CGTATTTTTG CCTTTTCTTT CTTGCCGTCC
 651  ACTGCGCCAT CCTTCCCTTC ACCCACCCGG AACCCTGAGG TGAGAACGCC
 701  CAAGTCAGCA ACTCAGCCAC AAACAACAGA AACTAATCTC CAAACTGCTC
 751  CTAAACTTTC TACATCTACA TCCACCACTG GGACAAGCCA TCTTGTAAAA
 801  TGTGCGGAGA AGGAGAAAAC TTTCTGTGTG AATGGAGGGG AGTGCTTCAT
 851  GGTGAAAGAC CTTTCAAACC CCTCGAGATA CTTGTGCAAA GGCGGAGGAG
 901  CTGTACCAGA AGAGAGTGCT GACCATAACC GGCATCTGCA TCGCCCTCCT
 951  TGTGGTCGGC ATCATGTGTG TGGTGGCCTA CTGCAAAACC AAGAAACAGC
1001  GGAAAAAGCT GCATGACCGT CTTCGGCAGA GCCTTCGGTC TGAACGAAAC
1051  AATACGATGA ACATTGCCAA TGGGCCTCAC CATCCTAACC CACCCCCCGA
1101  GAATGTCCAG CTGGTGAATC AATACGTATC TAAAAACGTC ATCTCCAGTG
1151  AGCATATTGT TGAGAGAGAA GCAGAGACAT CCTTTTCCAC CAGTCACTAT
1201  ACTTCCACAG CCCATCACTC CACTACTGTC ACCCAGACTC CTAGCCACAG
1251  CTGGAGCAAC GGACACACTG AAAGCATCCT TTCCGAAAGC CACTCTGTAA
1301  TCGTGATGTC ATCCGTAGAA AACAGTAGGC ACAGCAGCCC AACTGGGGCC
1351  G
```

FIGURE 4

```
  1  ACKMLYHLVG GASAW*WTVR AARPSSGGEP MEIYSPDMSE VAAERSSSPS
 51  TQLSADPSLD GLPAAEDMPE PQTEDGRTPG LVGLAVPCCA CLEAERLRGC
101  LNSEKICIVP ILACLVSLCL CIAGLKWVFV DKIFEYDSPT HLDPGGLGQD
151  PIISLDATAA SAVWVSSEAY TSPVSRAQSE SEVQVTVQGD KAVVSFEPSA
201  APTPKNRIFA FSFLPSTAPS FPSPTRNPEV RTPKSATQPQ TTETNLQTAP
251  KLSTSTSTTG TSHLVKCAEK EKTFCVNGGE CFMVKDLSNP SRYLCKGGGA
301  VPEESADHNR HLHRPPCGRH HVCGGLLQNQ ETAEKAA*PS SAEPSV*TKQ
351  YDEHCQWASP S*PTPRECPA GESIRI*KRH LQ*AYC*ERS RDILFHQSLY
401  FHSPSLHYCH PDS*PQLEQR TH*KHPFRKP LCNRDVIRRK Q*AQQPNWG
```

FIGURE 5A

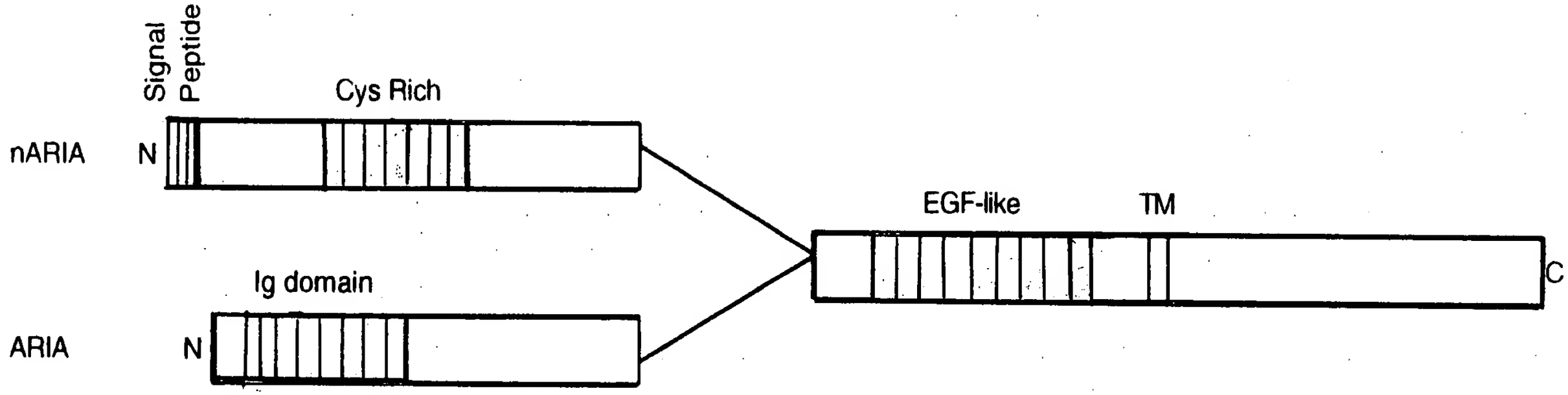
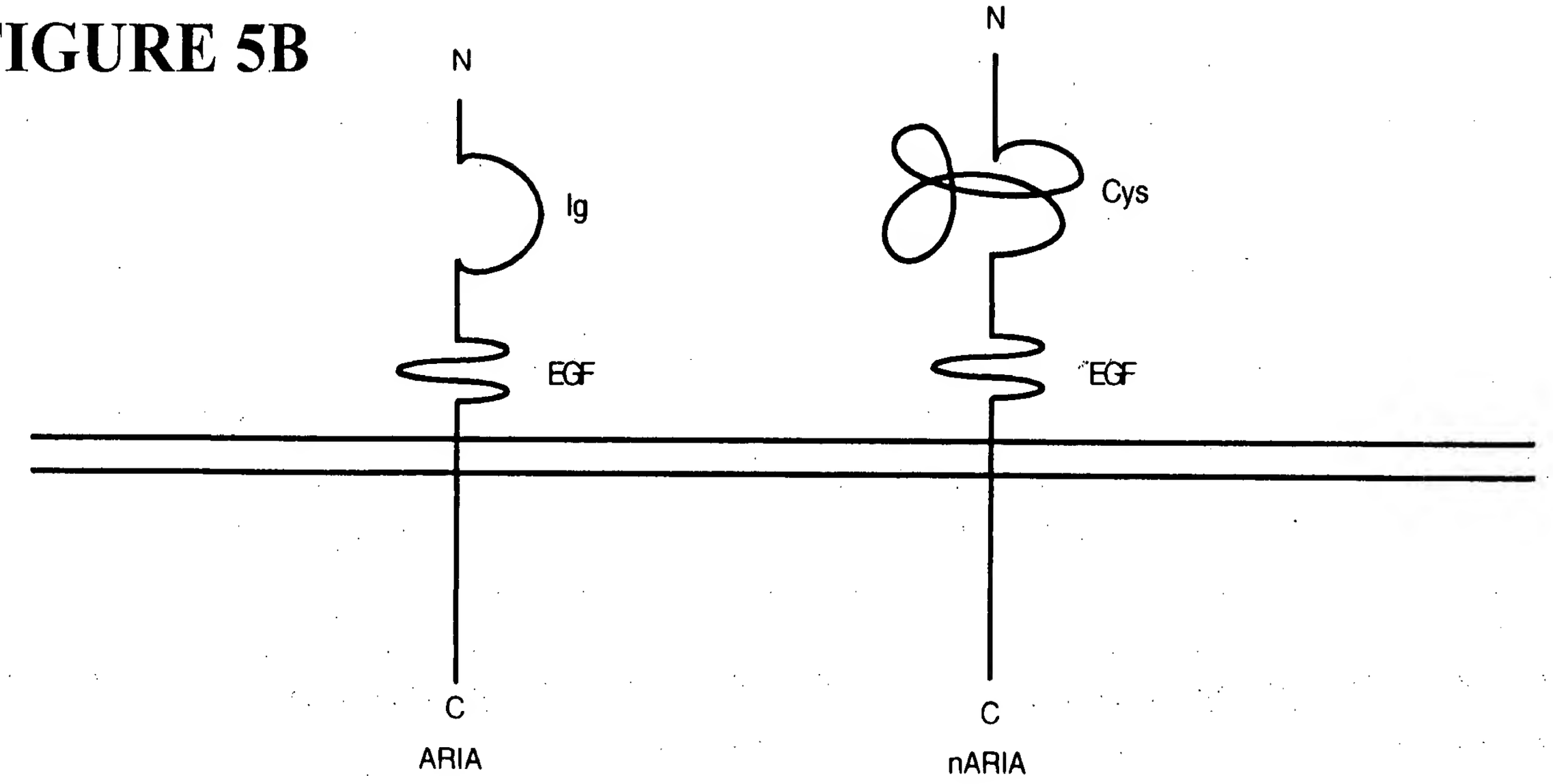


FIGURE 5B



Title: A-FORM OF CYTOPLASMIC DOMAIN OF nARIA (CRD-NEUREGULIN) AND USES THEREOF
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FIGURE 6

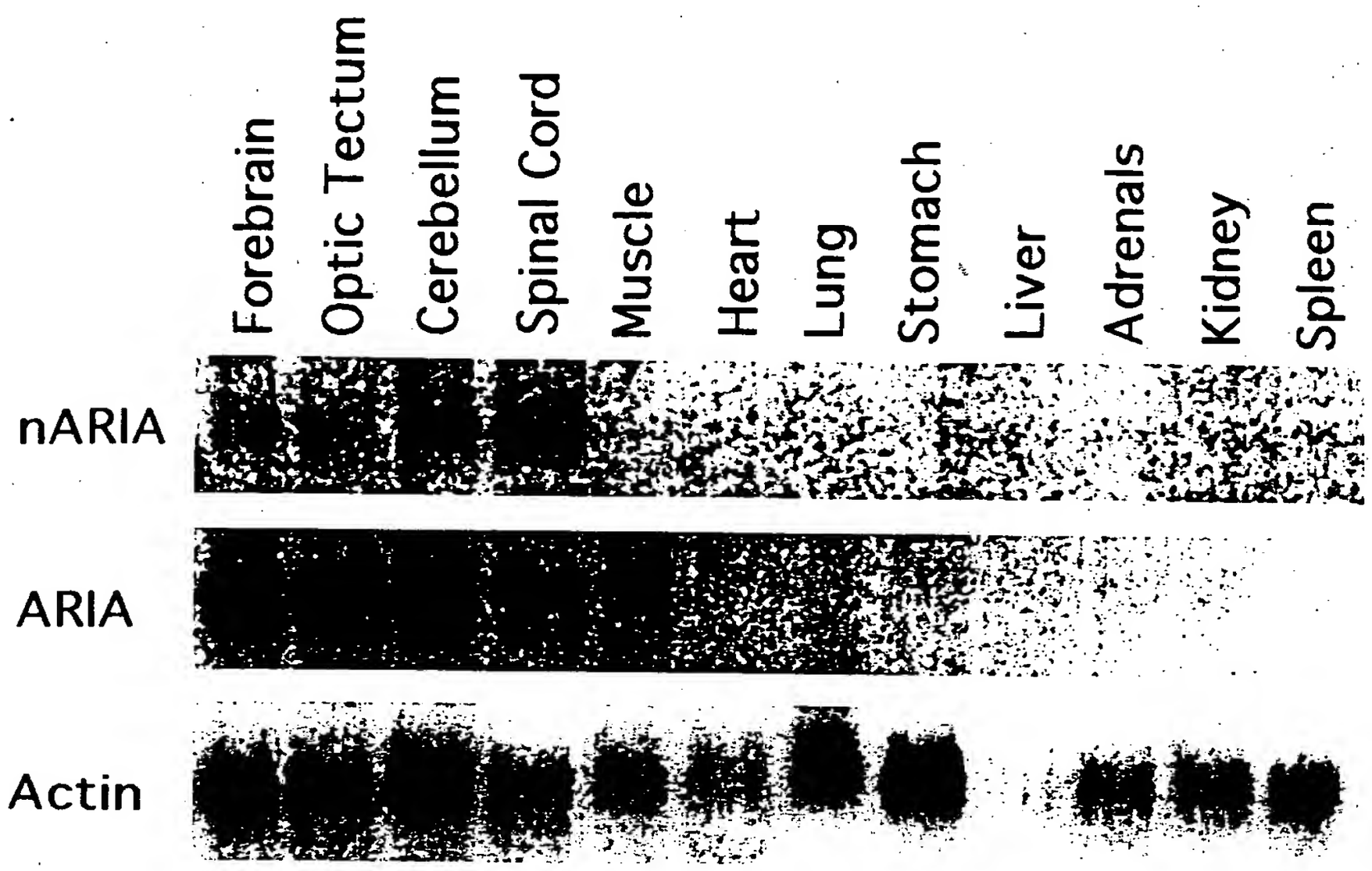

Forebrain
Optic Tectum
Cerebellum
Spinal Cord
Muscle
Heart
Lung
Stomach
Liver
Adrenals
Kidney
Spleen
nARIA
ARIA
Actin

FIGURE 7

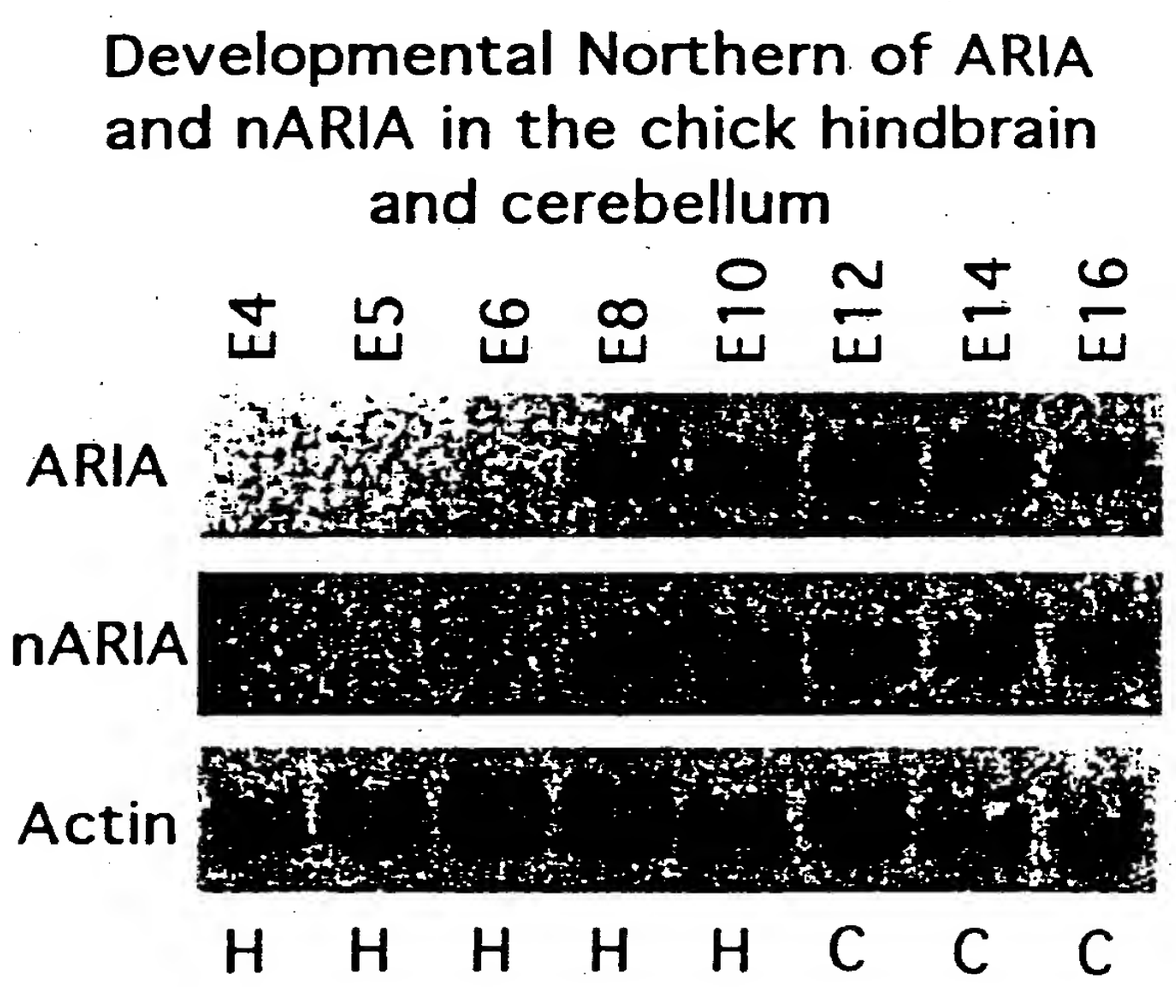

Developmental Northern of ARIA
and nARIA in the chick hindbrain
and cerebellum
E4
E5
E6
E8
E10
E12
E14
E16
ARIA
nARIA
Actin
H
H
H
H
H
C
C
C

FIGURE 8A

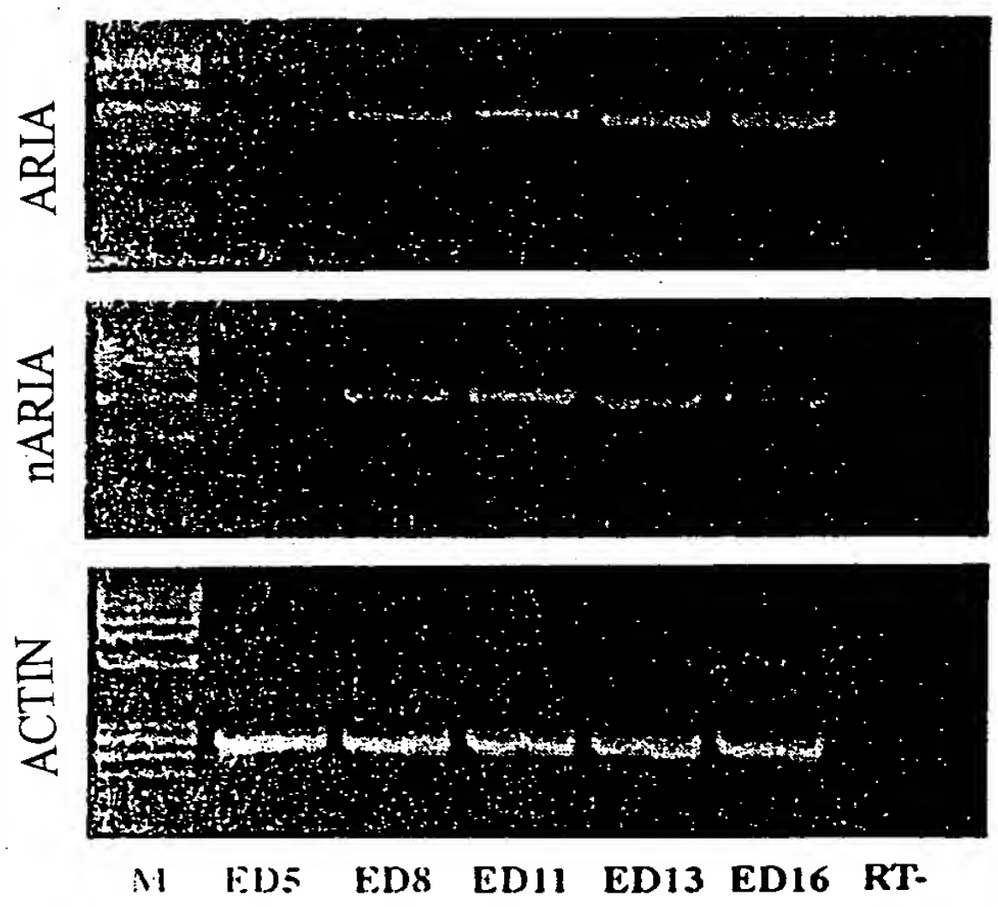


FIGURE 8B

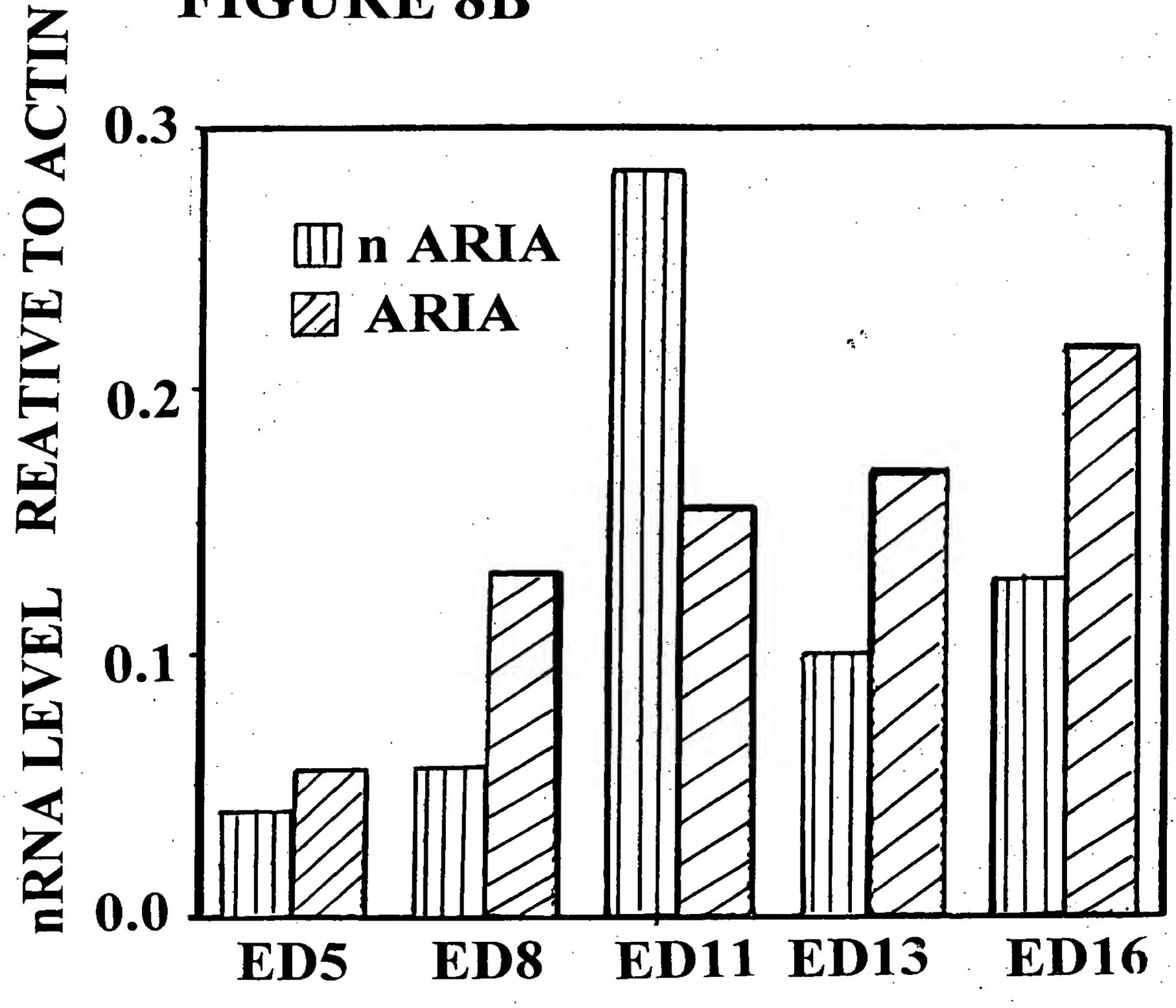

nRNA LEVEL REATIVE TO AC
0.3
0.2
0.1
0.0
n ARIA
ARIA
ED5
ED8
ED11
ED13
ED16

FIGURE 9A

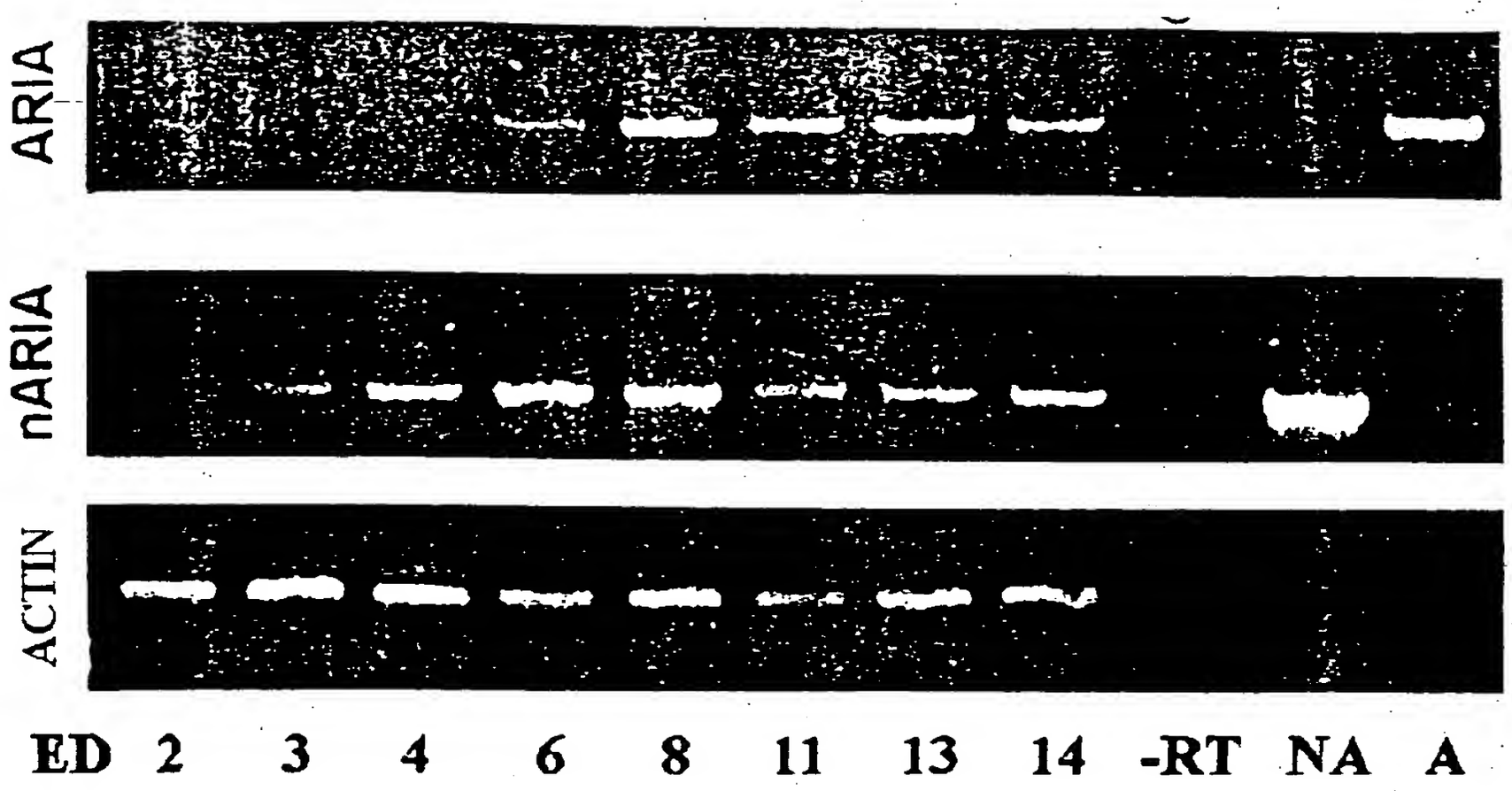


FIGURE 9B

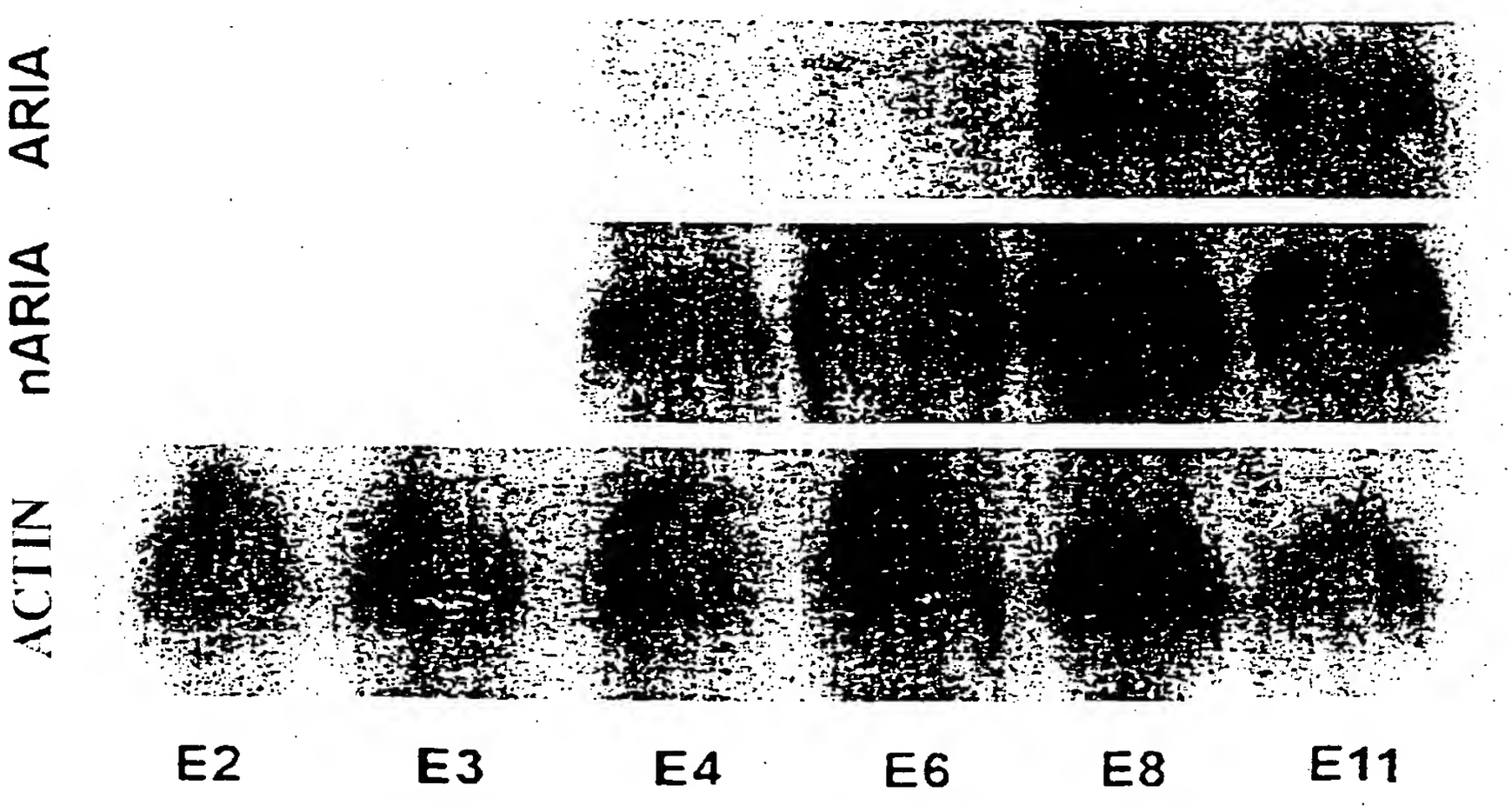


FIGURE 9C

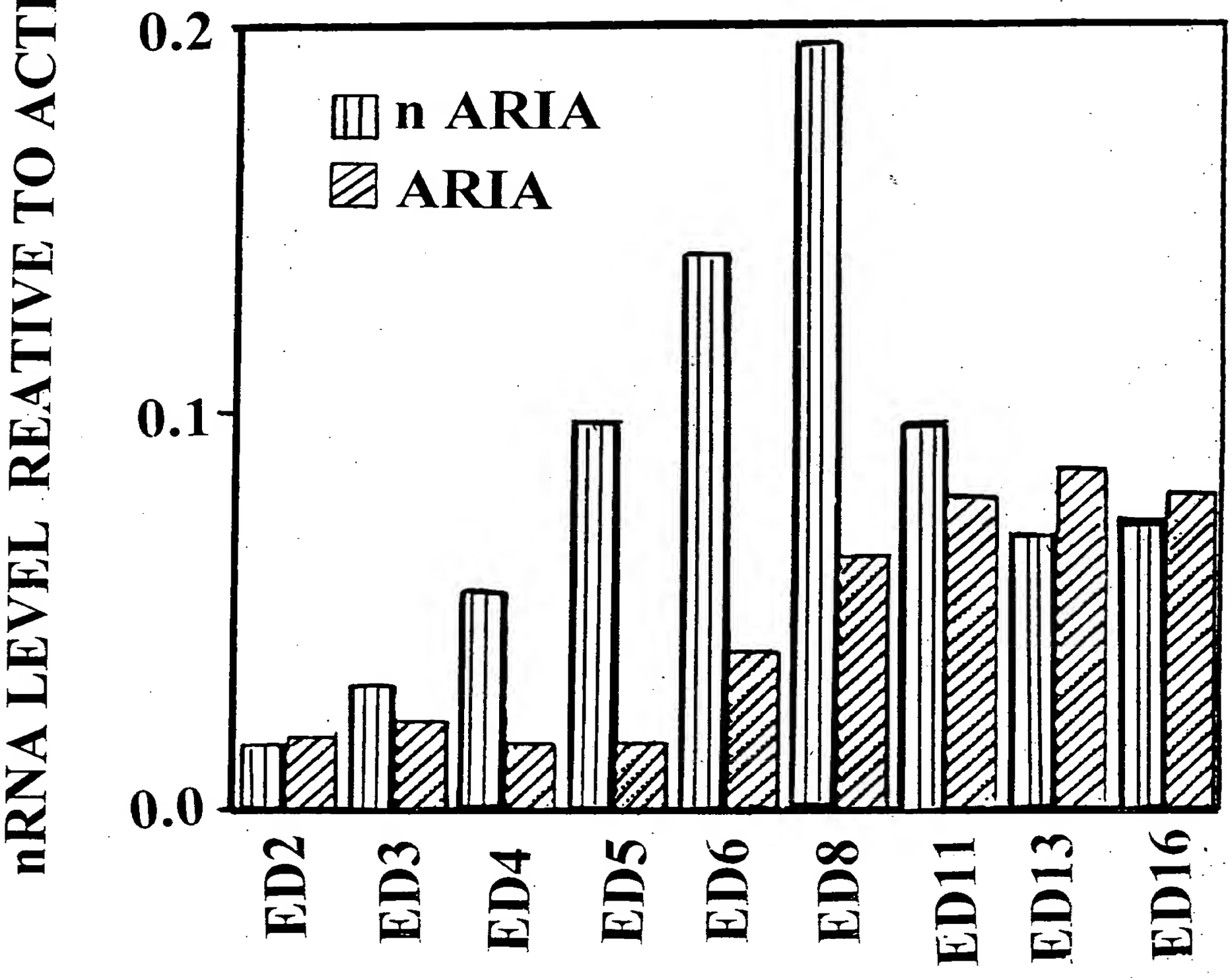
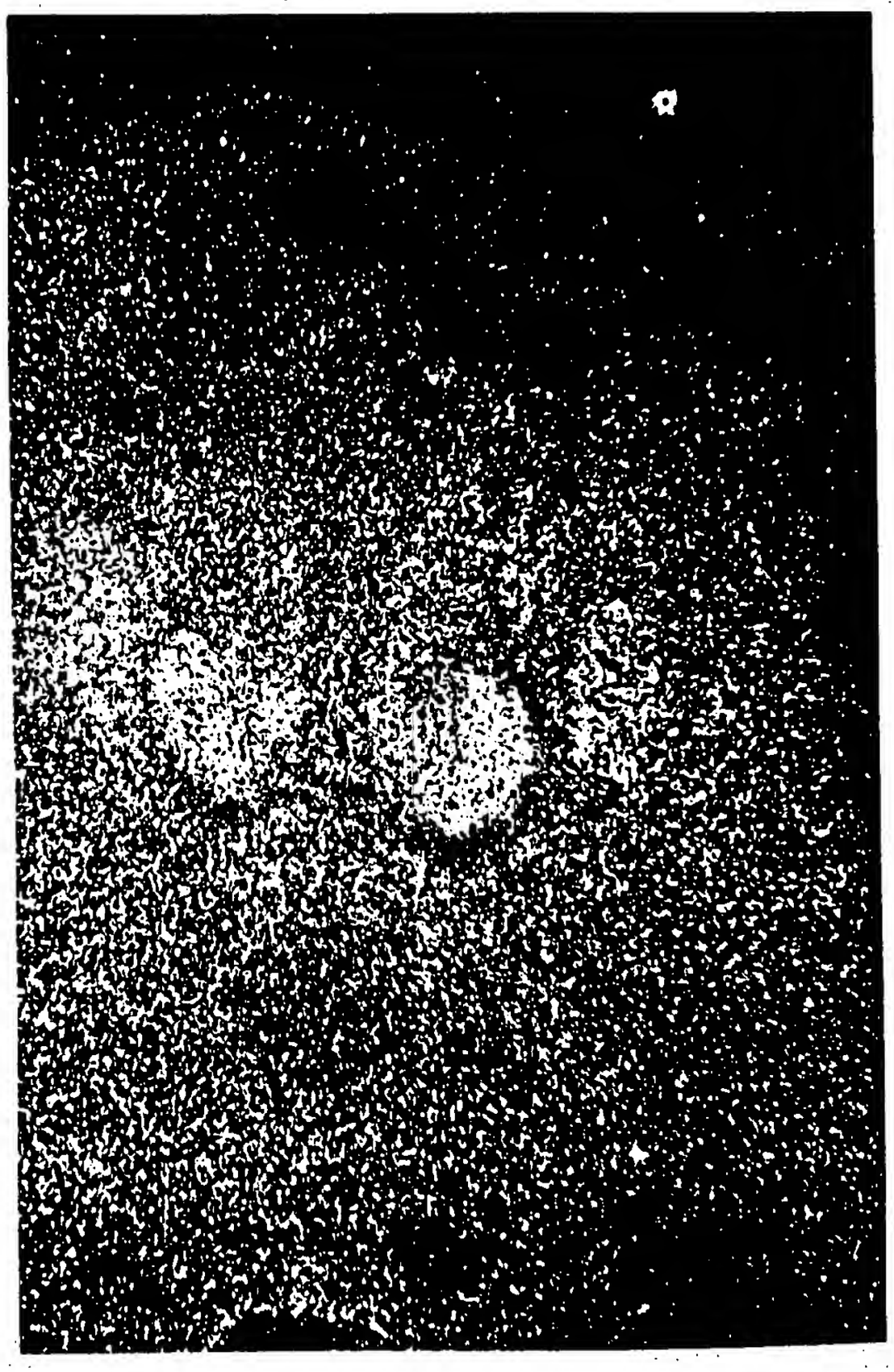

nRNA LEVEL REATIVE TO ACTIN
0.2
0.1
0.0
n ARIA
ARIA
ED2
ED3
ED4
ED5
ED6
ED8
ED11
ED13
ED16

FIGURE 10A

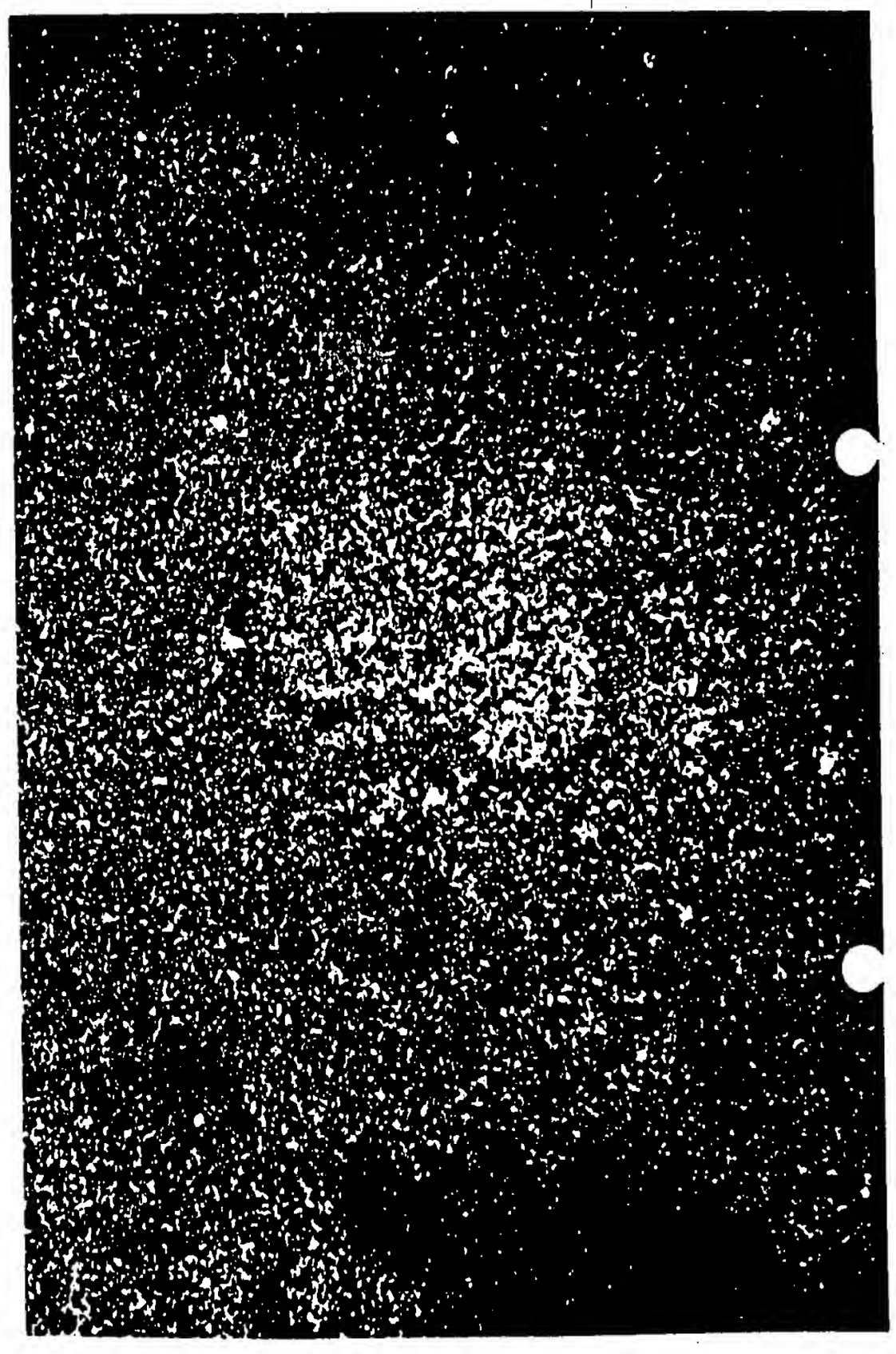
ED5 trunk cross-section



nARIA specific probe

FIGURE 10B

ED5 trunk cross-section



ARIA specific probe

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FIGURE 10C

nARIA specific probe

ED7 trunk cross-section

FIGURE 10D

ARIA specific probe

ED7 trunk cross-section

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FIGURE 11A

FIGURE 11B

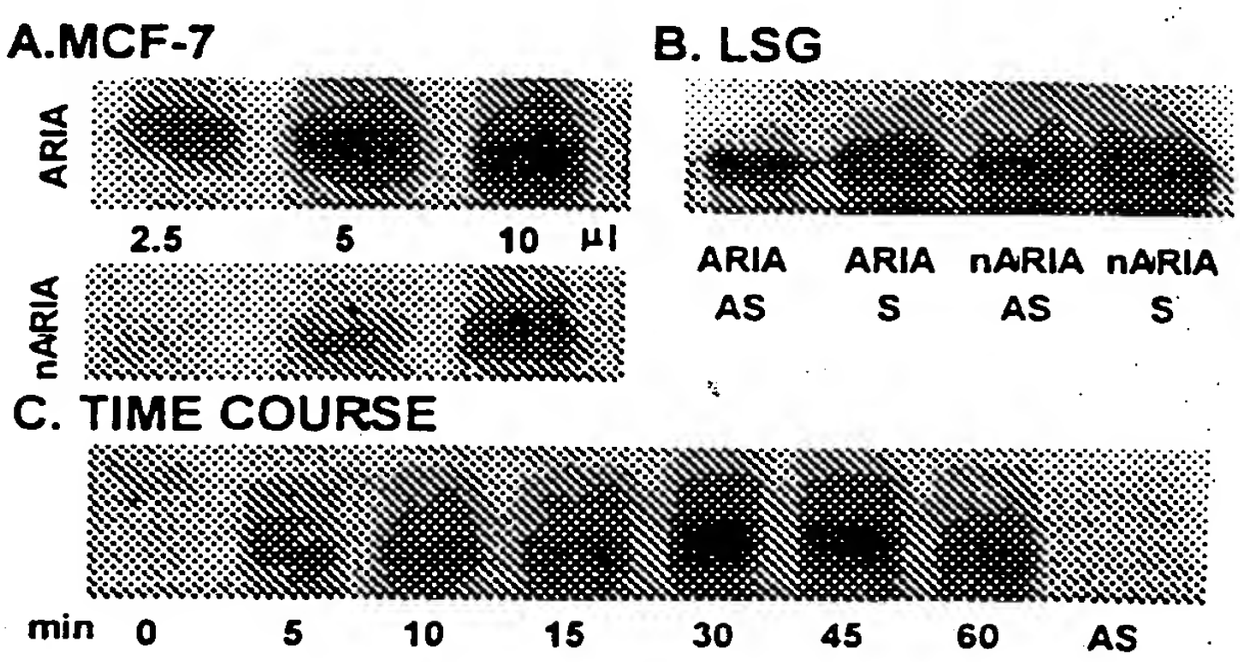


FIGURE 11C

FIGURE 12

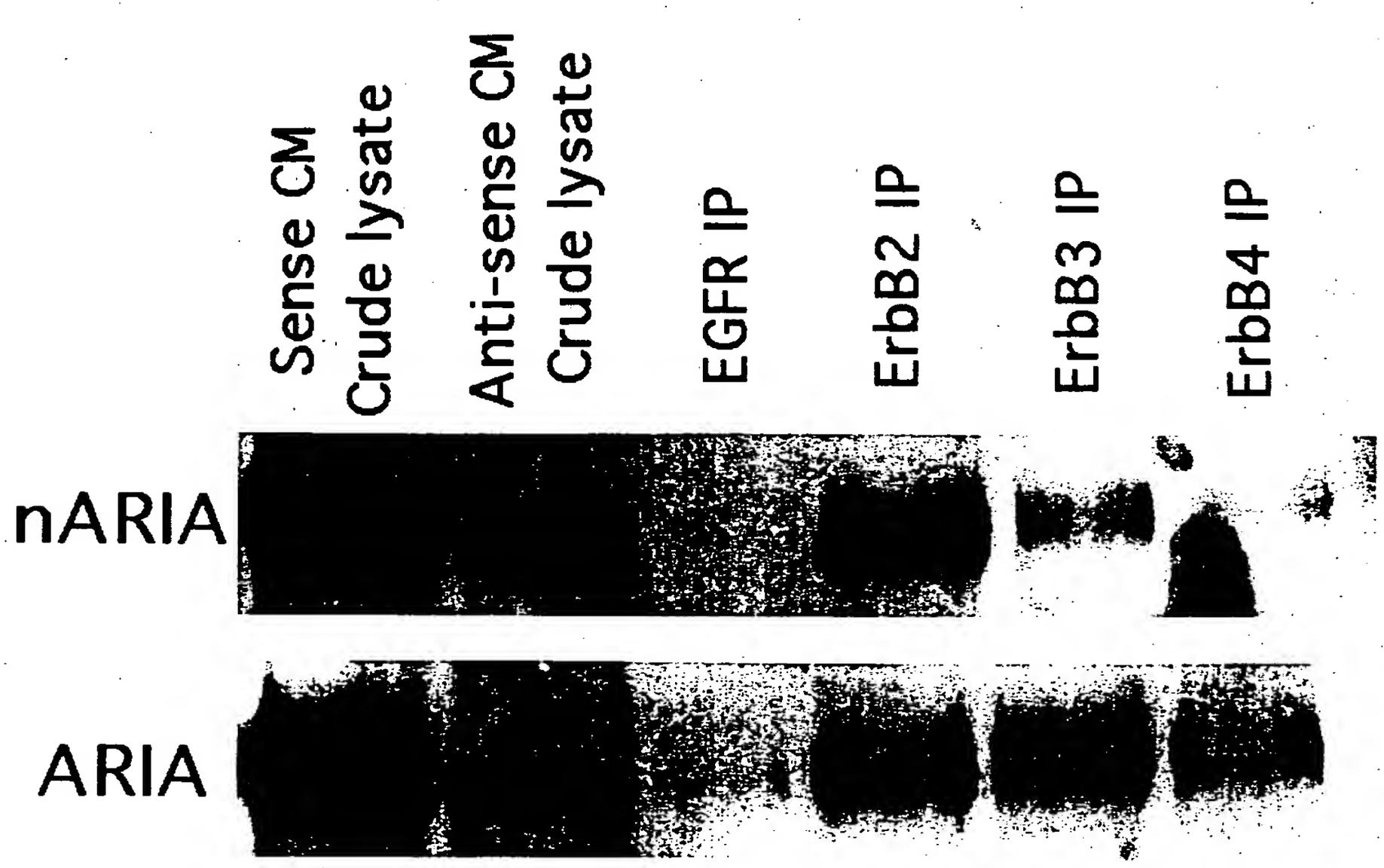

Sense CM
Crude lysate
Anti-sense CM
Crude lysate
EGFR IP
ErbB2 IP
ErbB3 IP
ErbB4 IP
nARIA
ARIA

FIGURE 13A

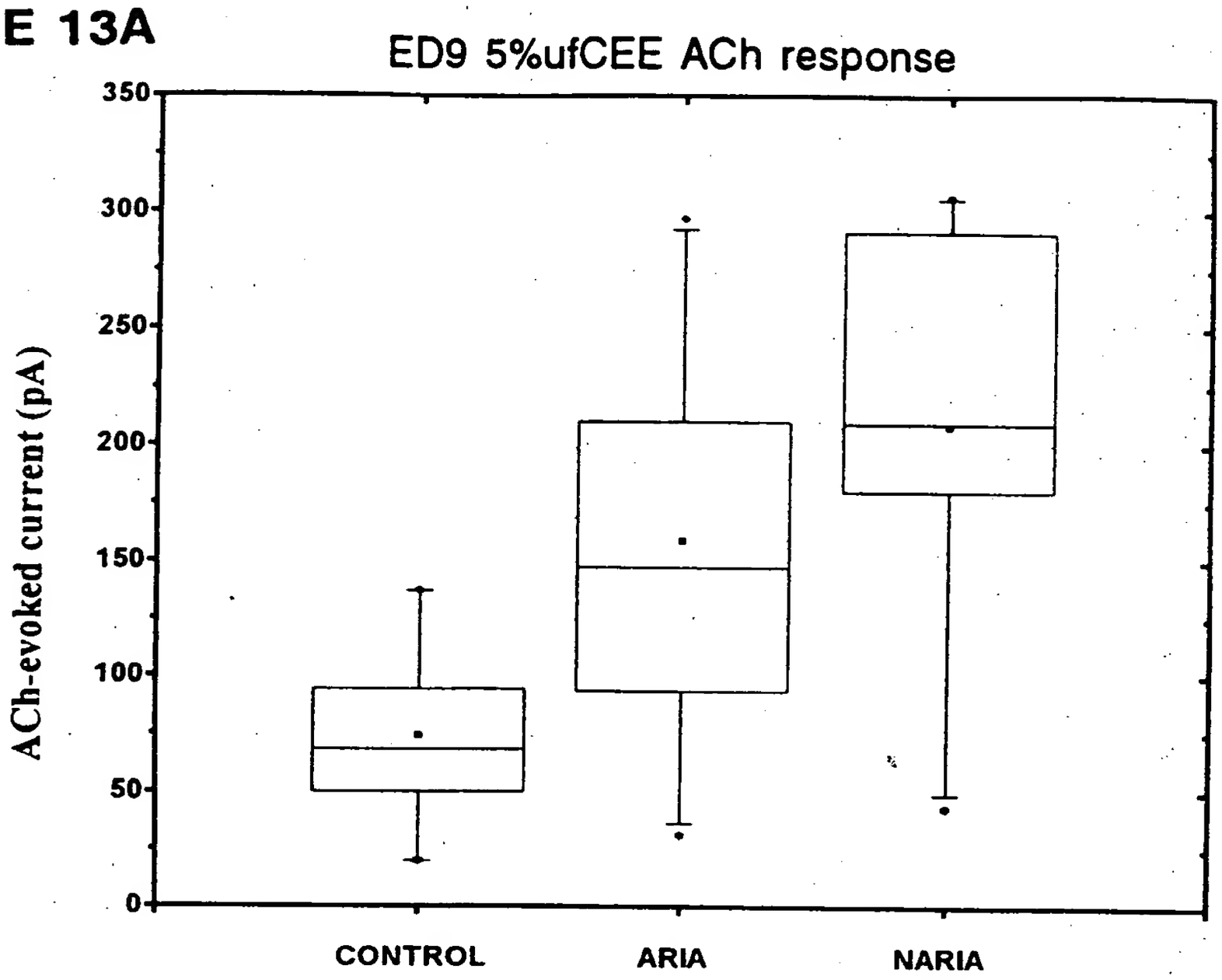
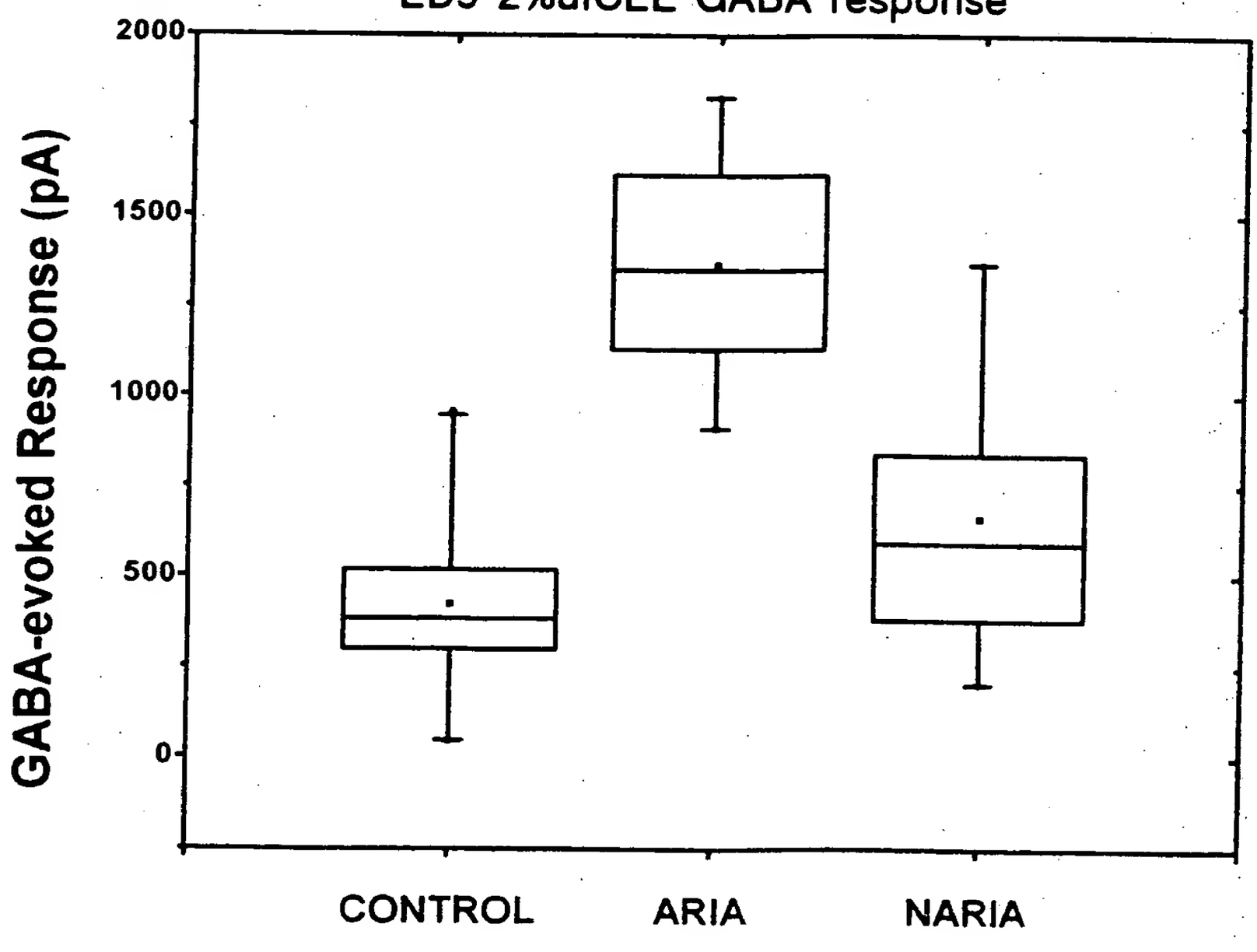
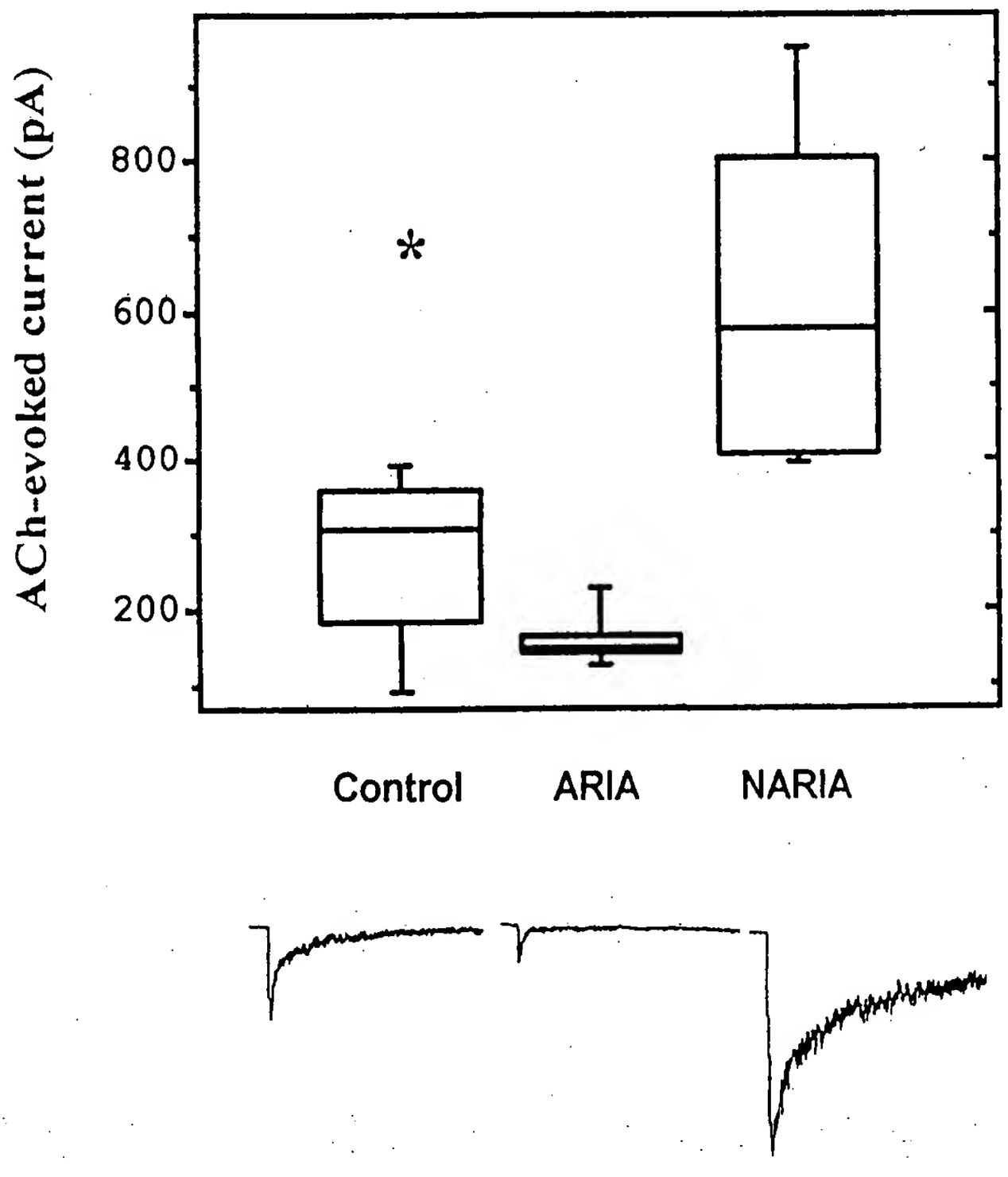


FIGURE 13B



ED 11

FIGURE 13C



ED11

FIGURE 13D

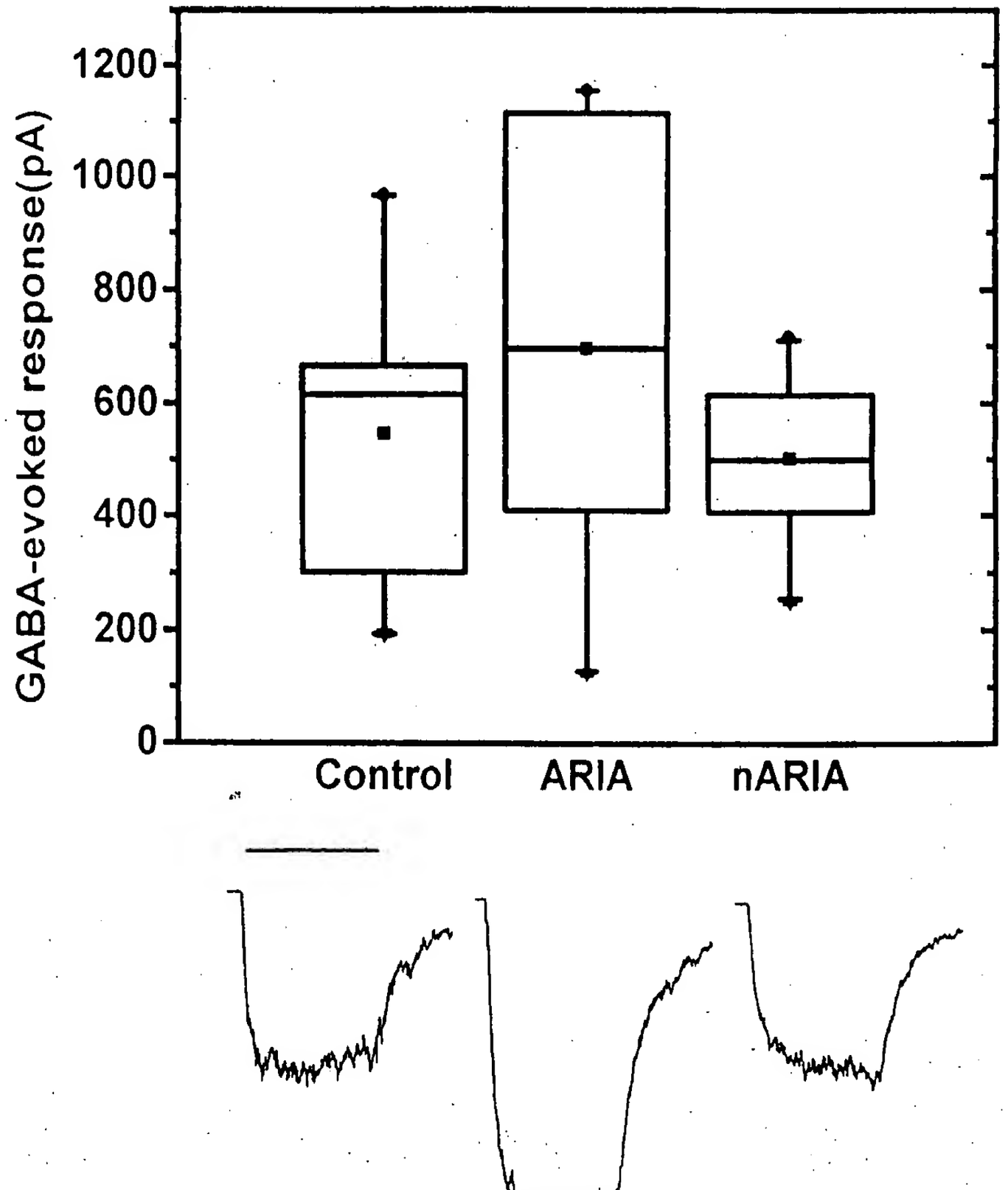


FIGURE 14A

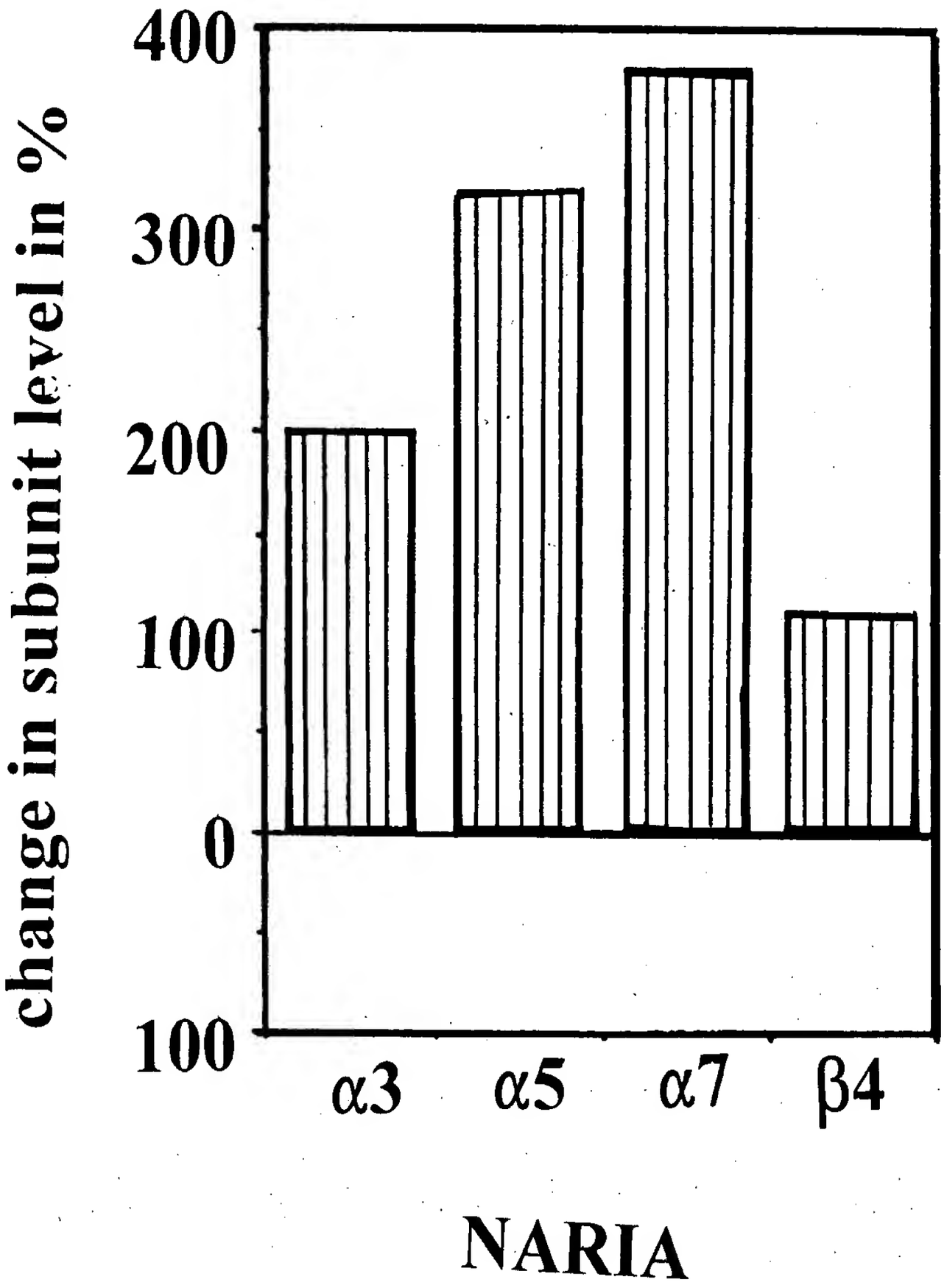


FIGURE 14B

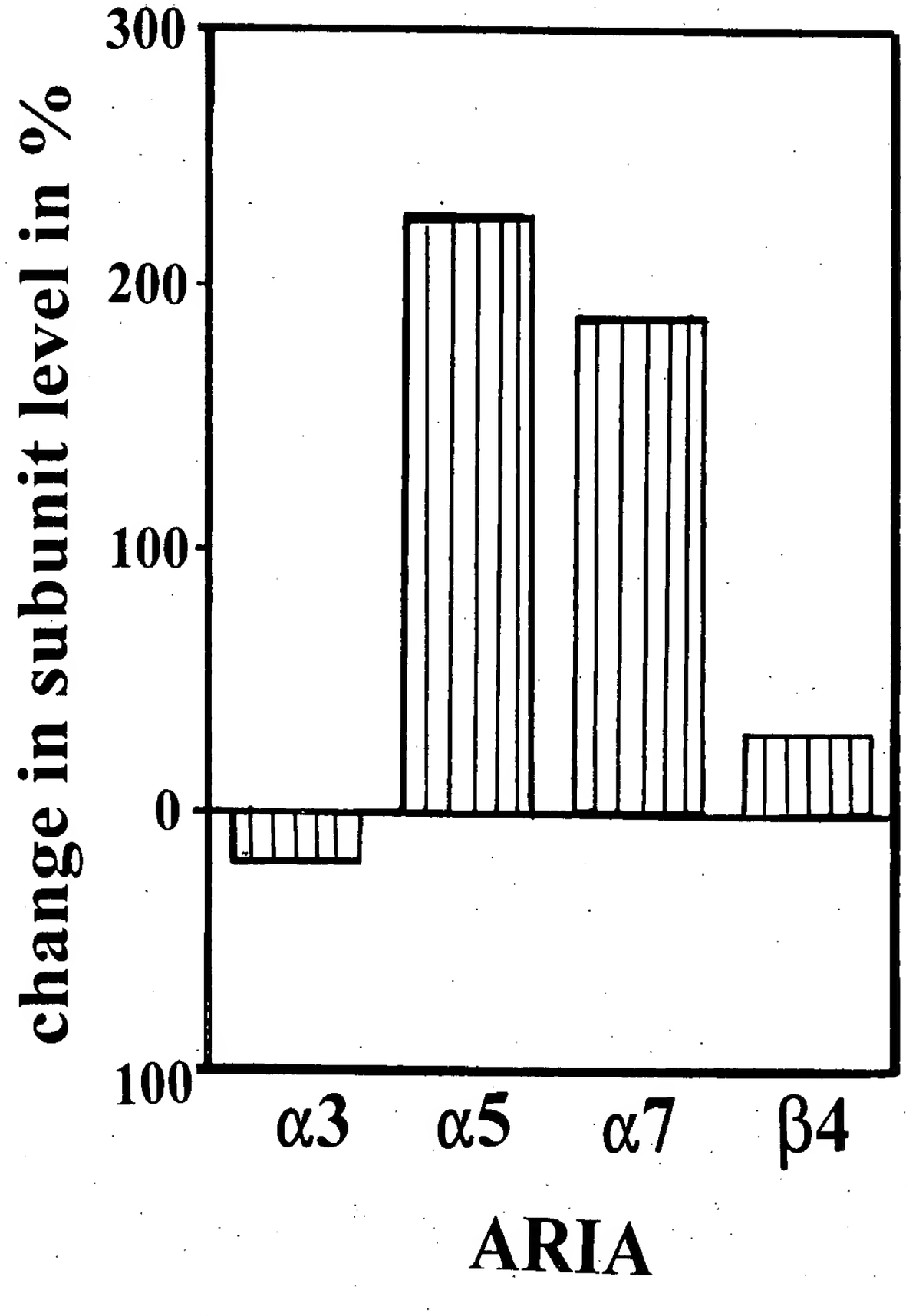


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FIGURE 15

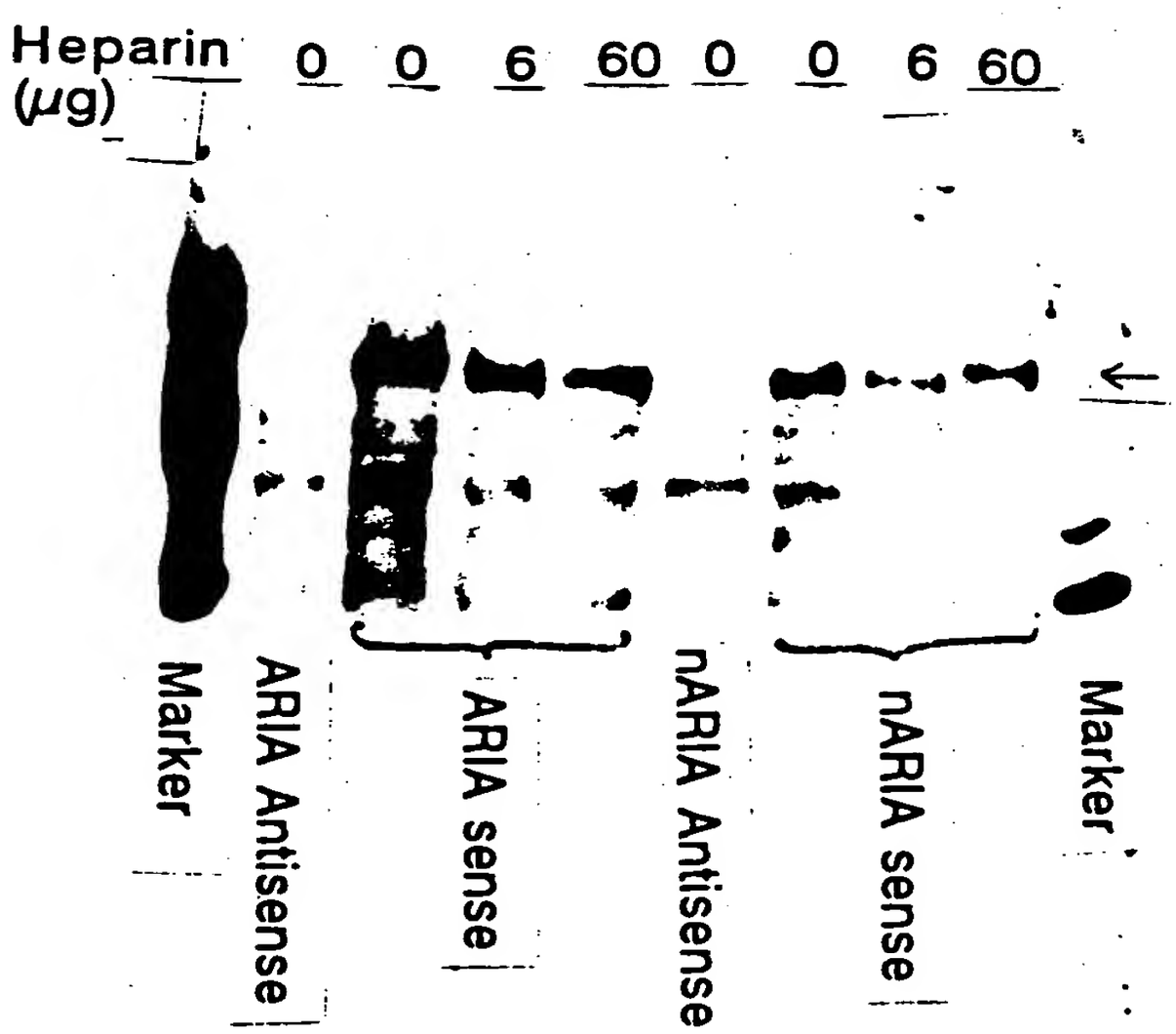

Heparin (μg)
0
0
6
60
0
0
6
60
Marker
ARIA Antisense
ARIA sense
nARIA Antisense
nARIA sense
Marker

FIGURE 16

FIGURE 17

FIG. 18

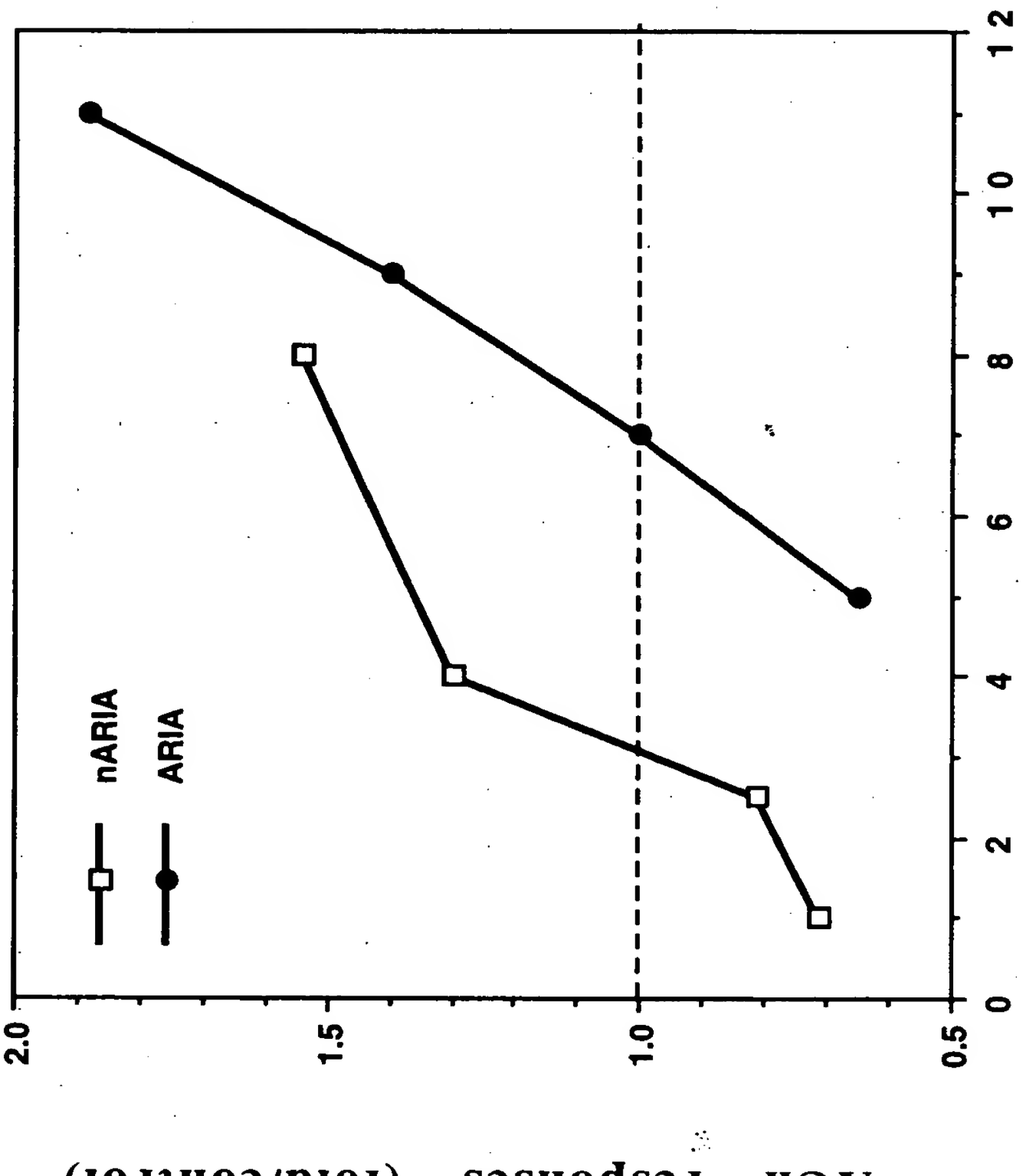
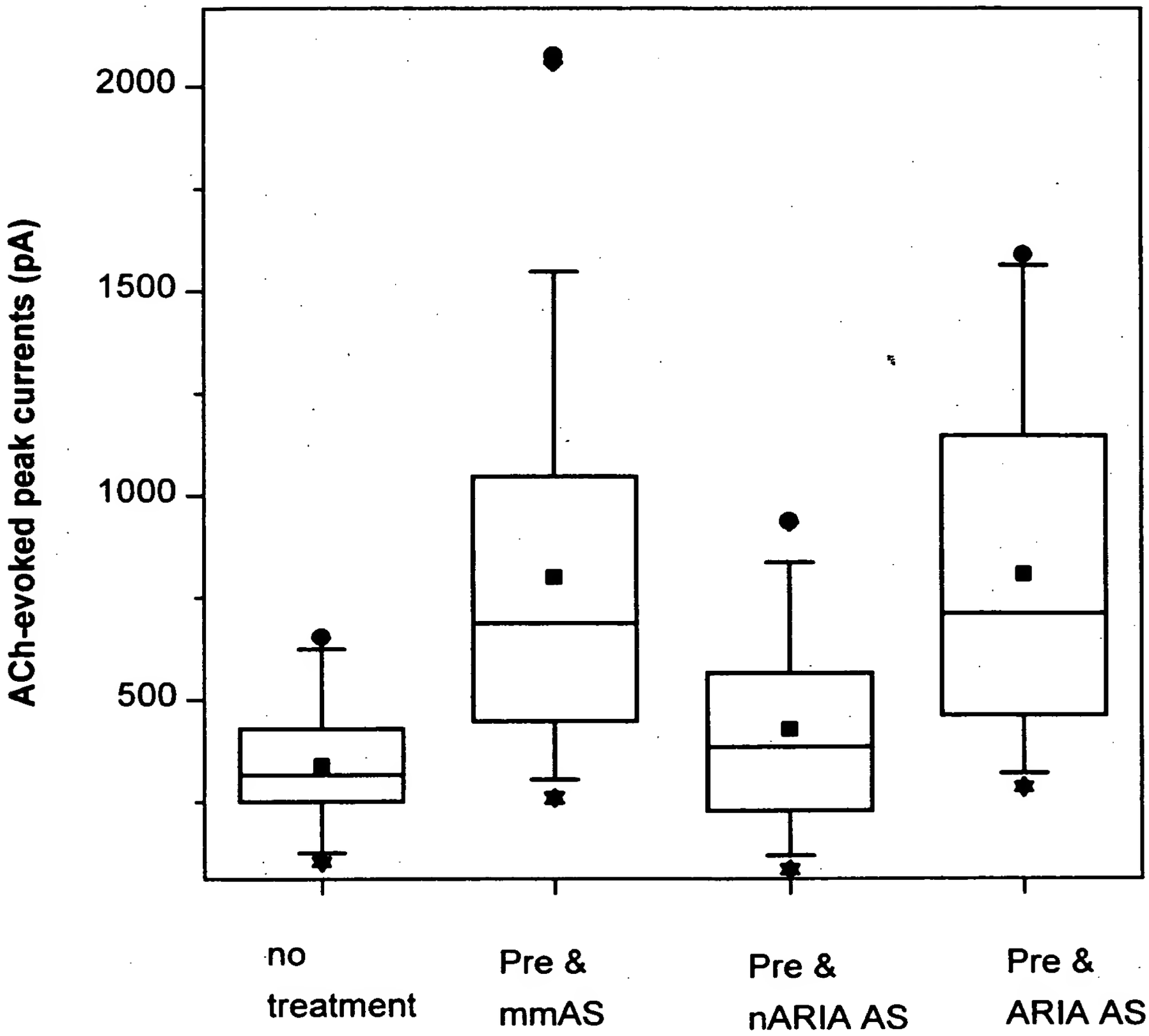

nARIA
ARIA
2.0
1.5
1.0
0.5
0
2
4
6
8
10
12
activity units
ACh responses (fold/control)

FIG. 19



no treatment=sympathetic neurons alone
'Pre'=treatment of sympathetic neurons with presynaptic input-conditioned media+various oligos
mmAS=mismatch antisense control
nARIA AS=nARIA specific antisense oligonucleotides
ARIA AS=ARIA specific antisense oligonucleotides

FIG. 20A

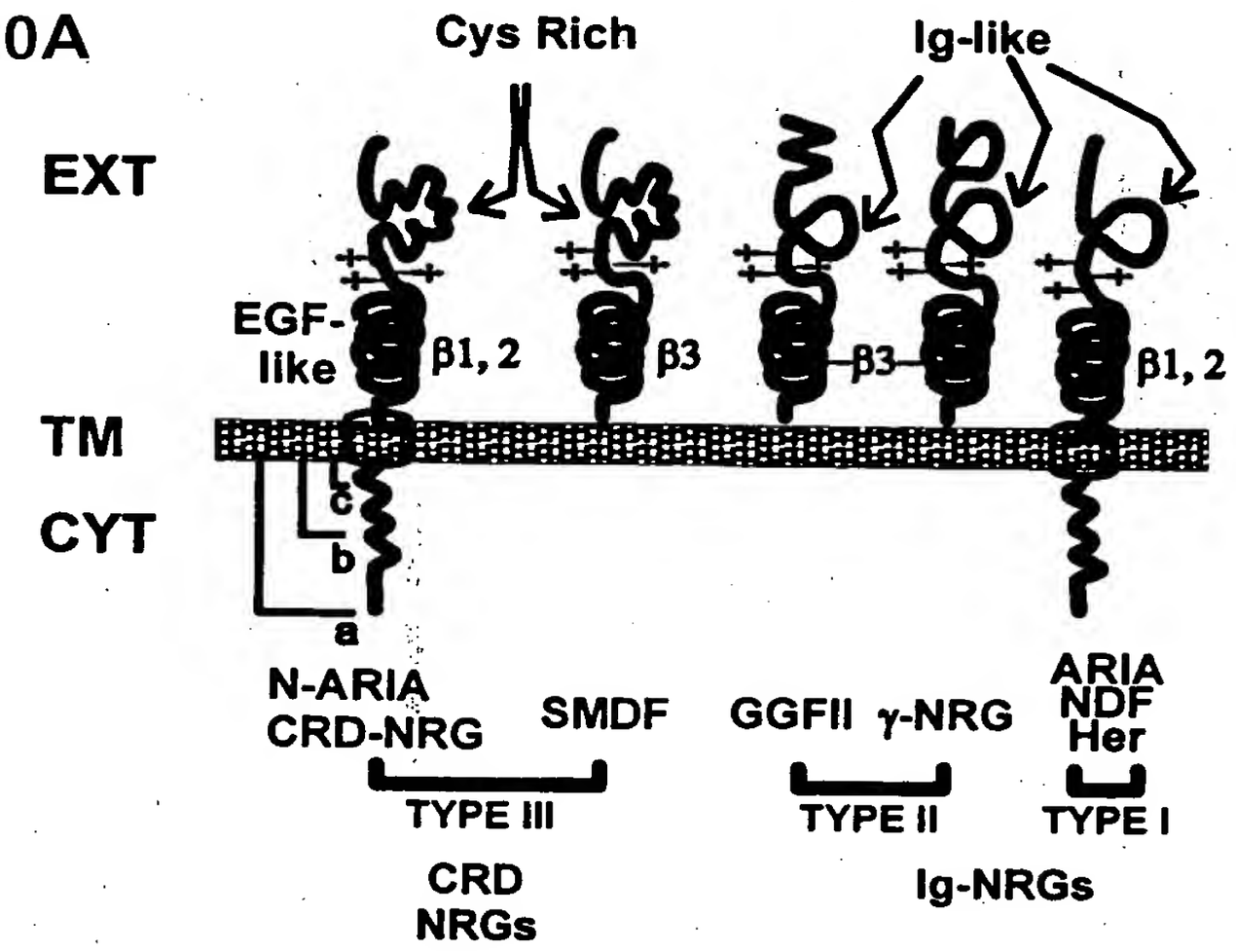


FIG. 20B

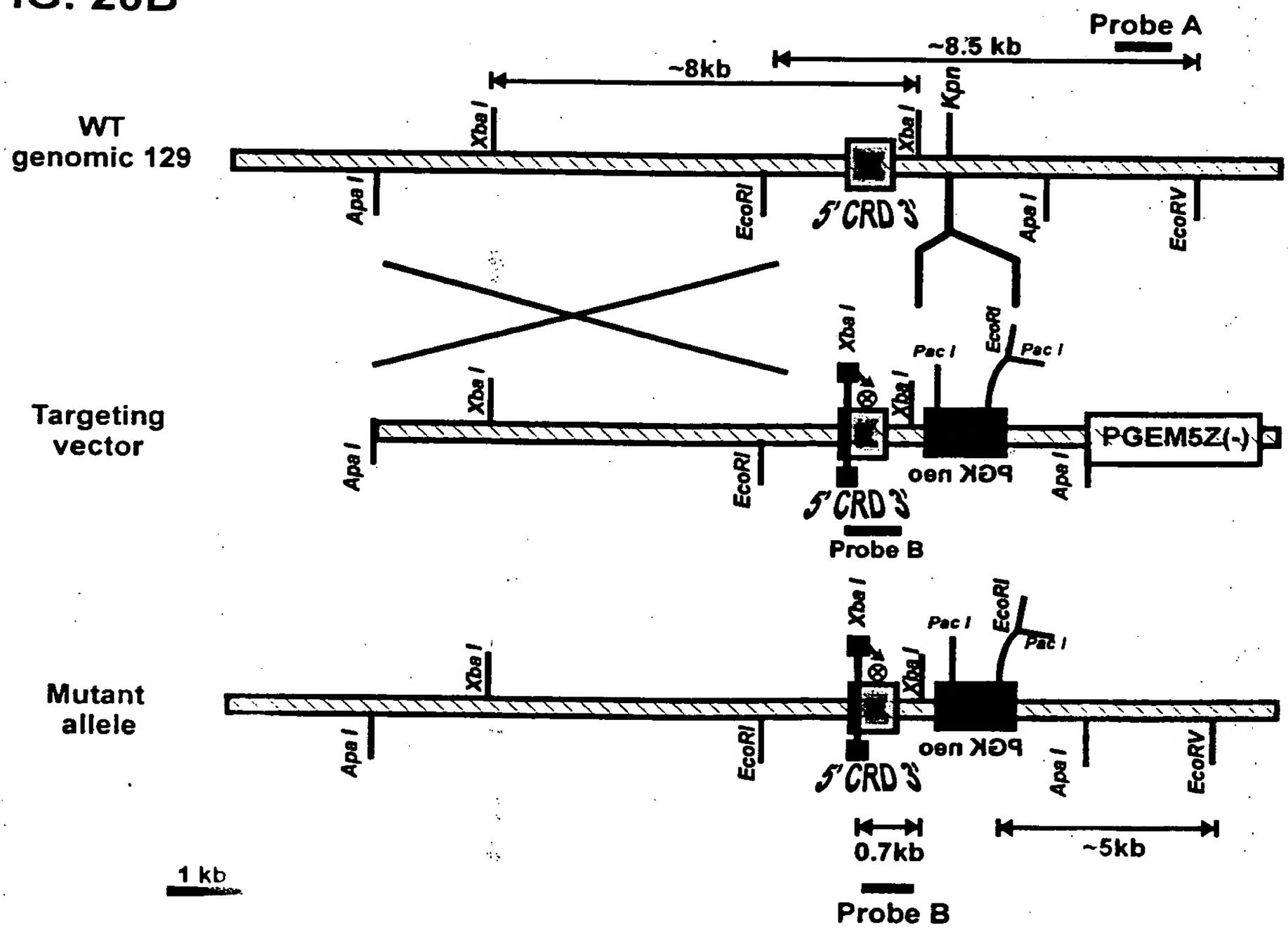


FIG. 20C

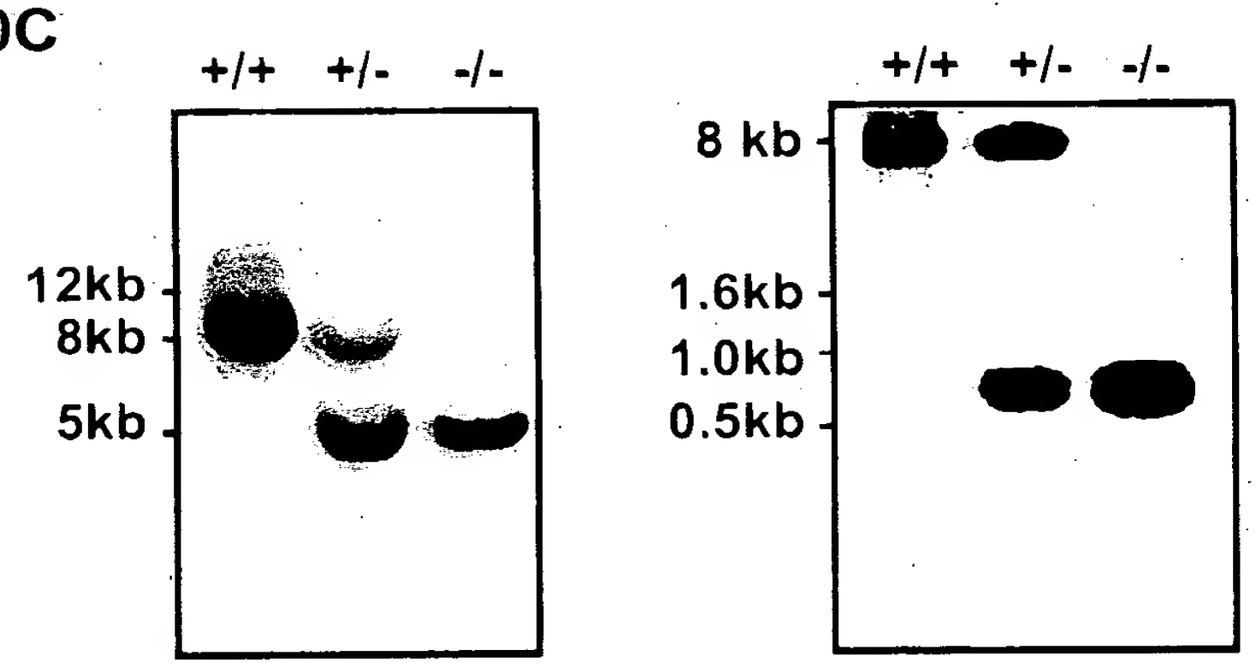


FIG. 20D

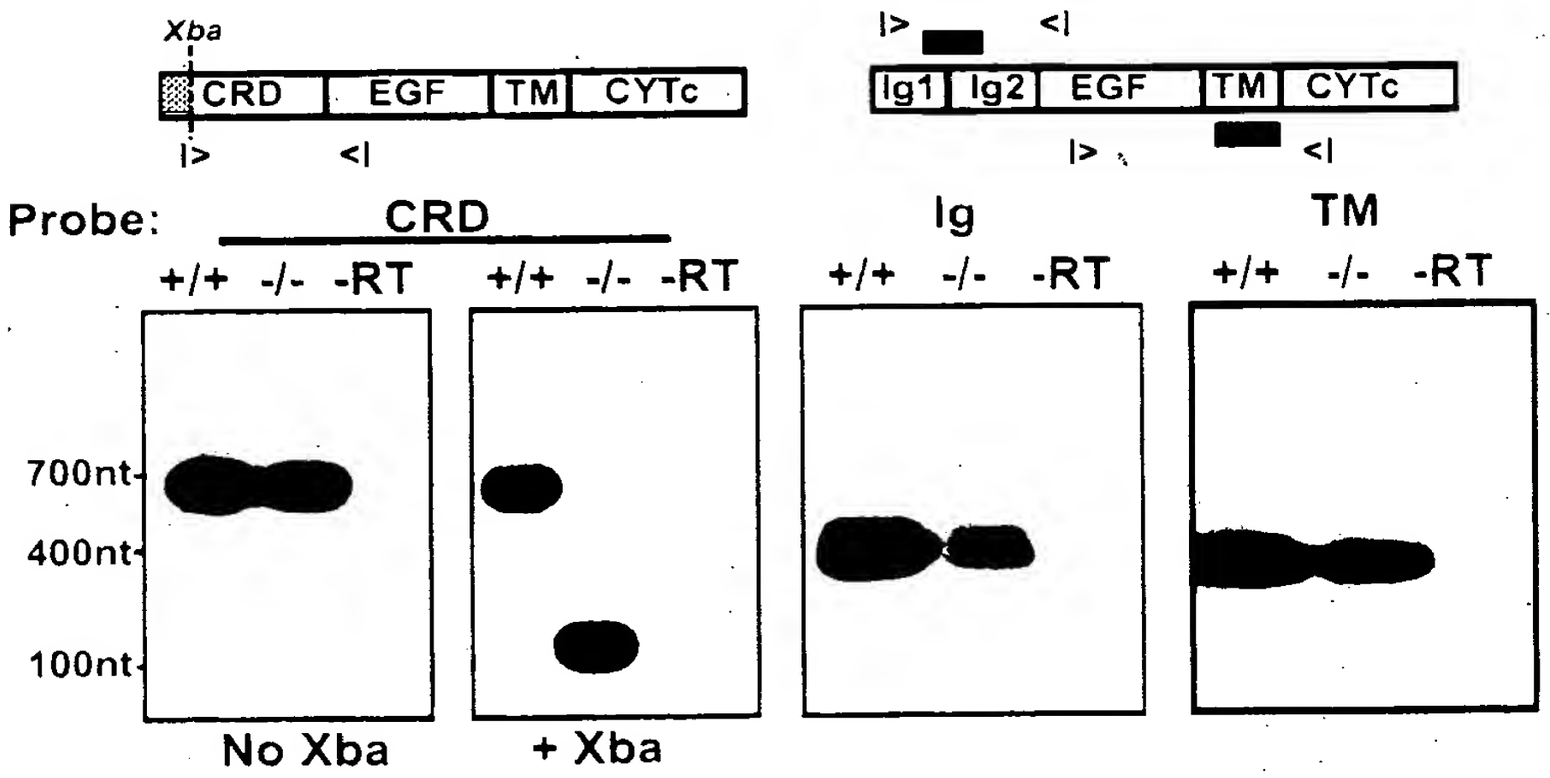


FIG. 20E

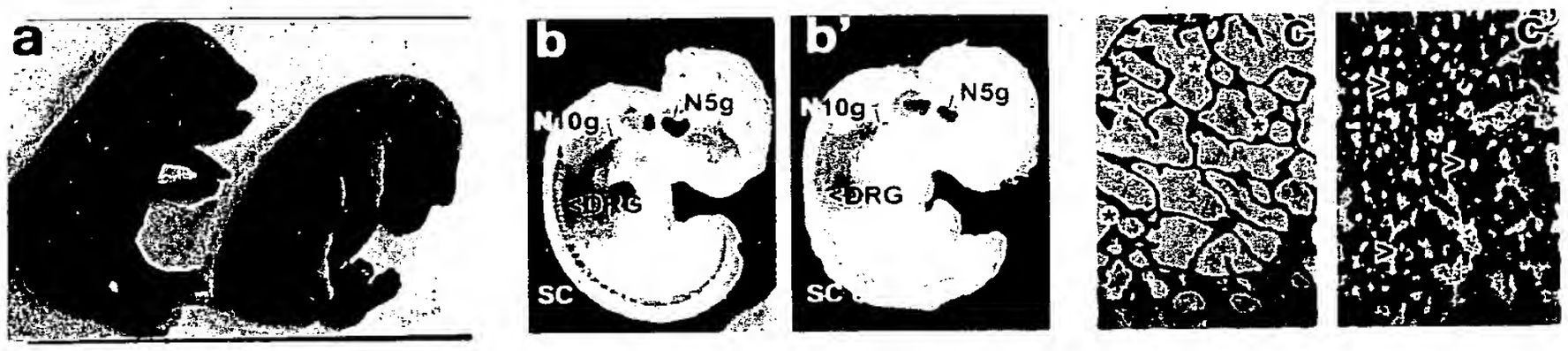


FIG. 21A

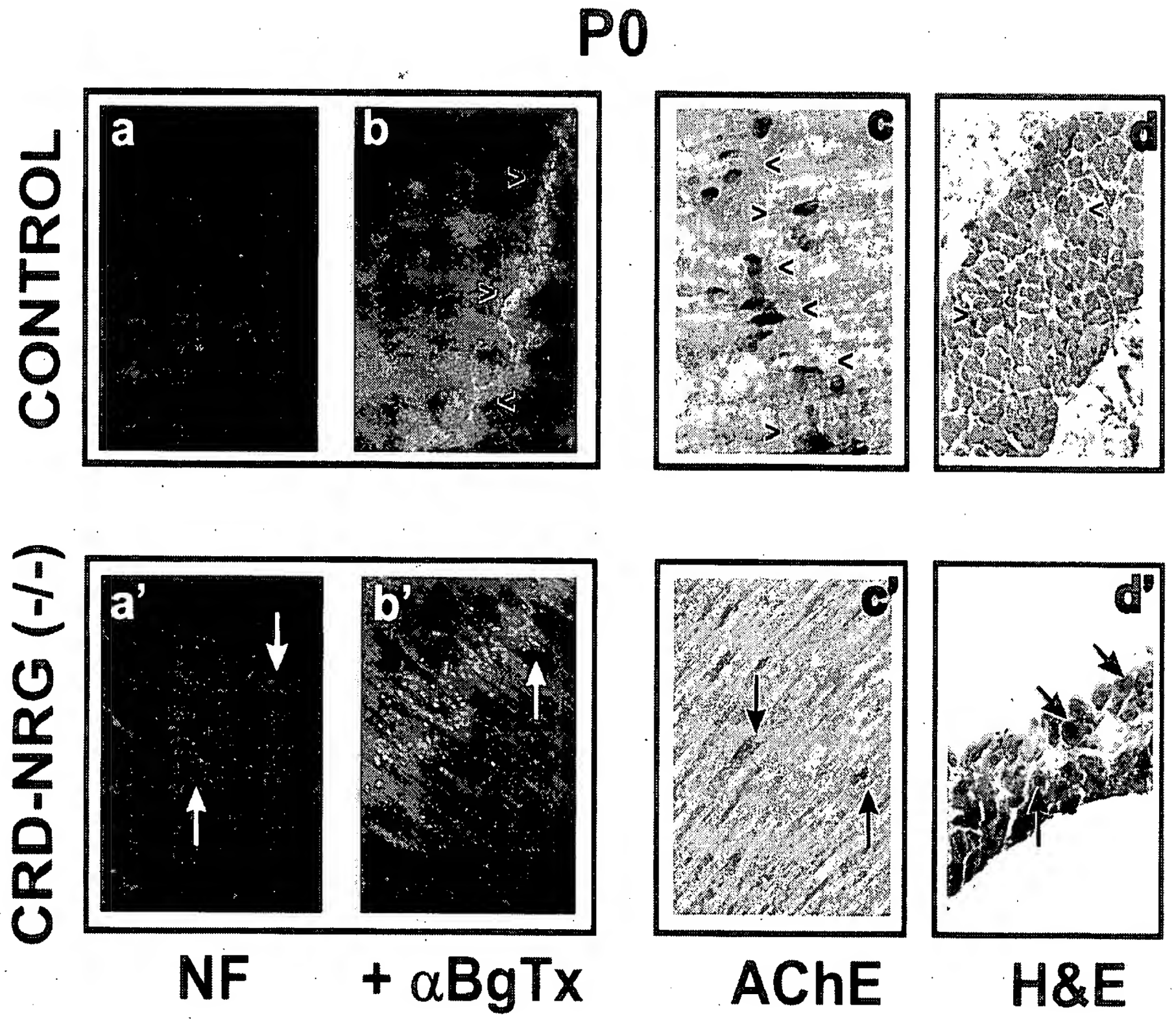


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FIG. 21B

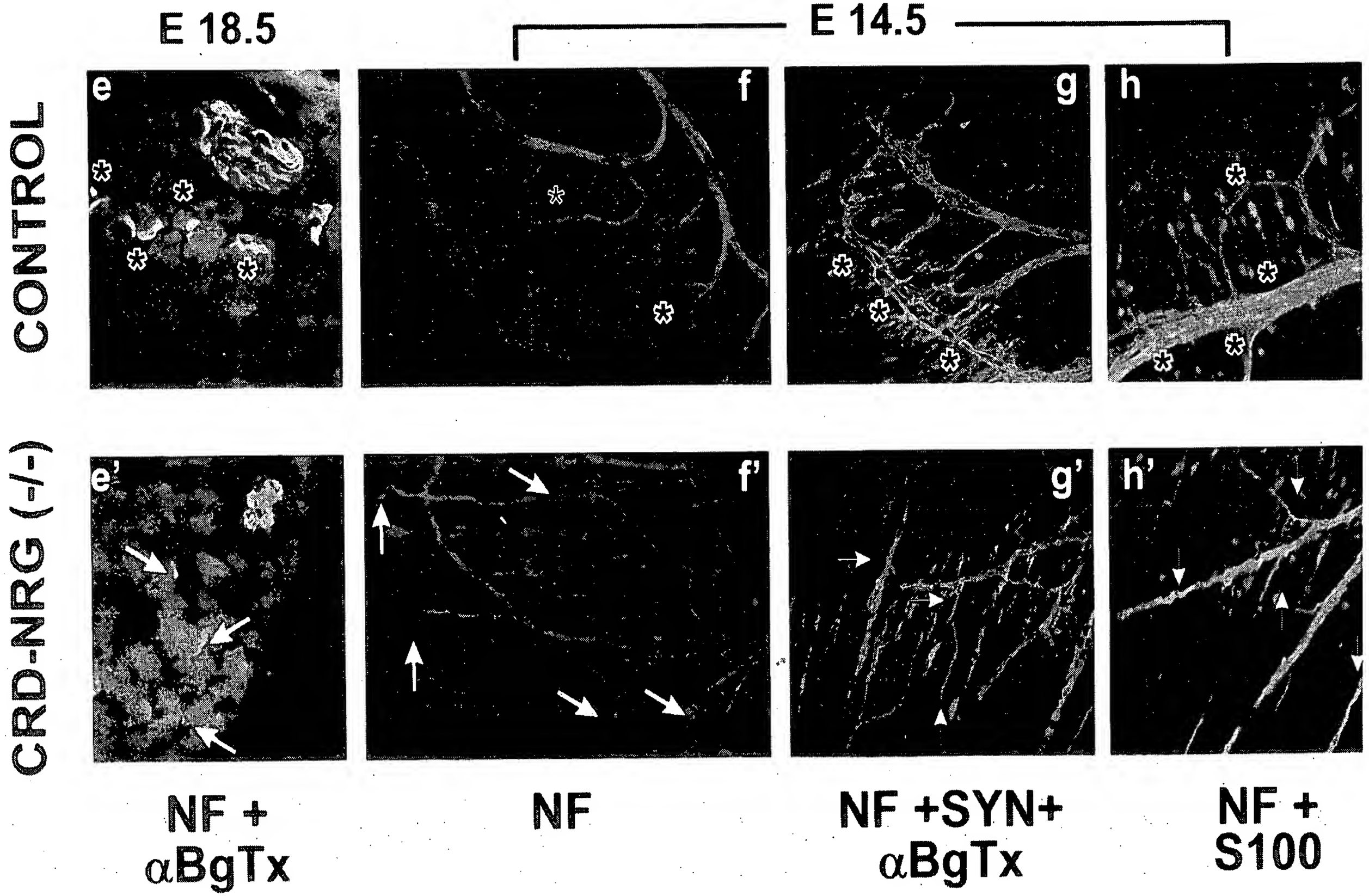

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FIG. 22A

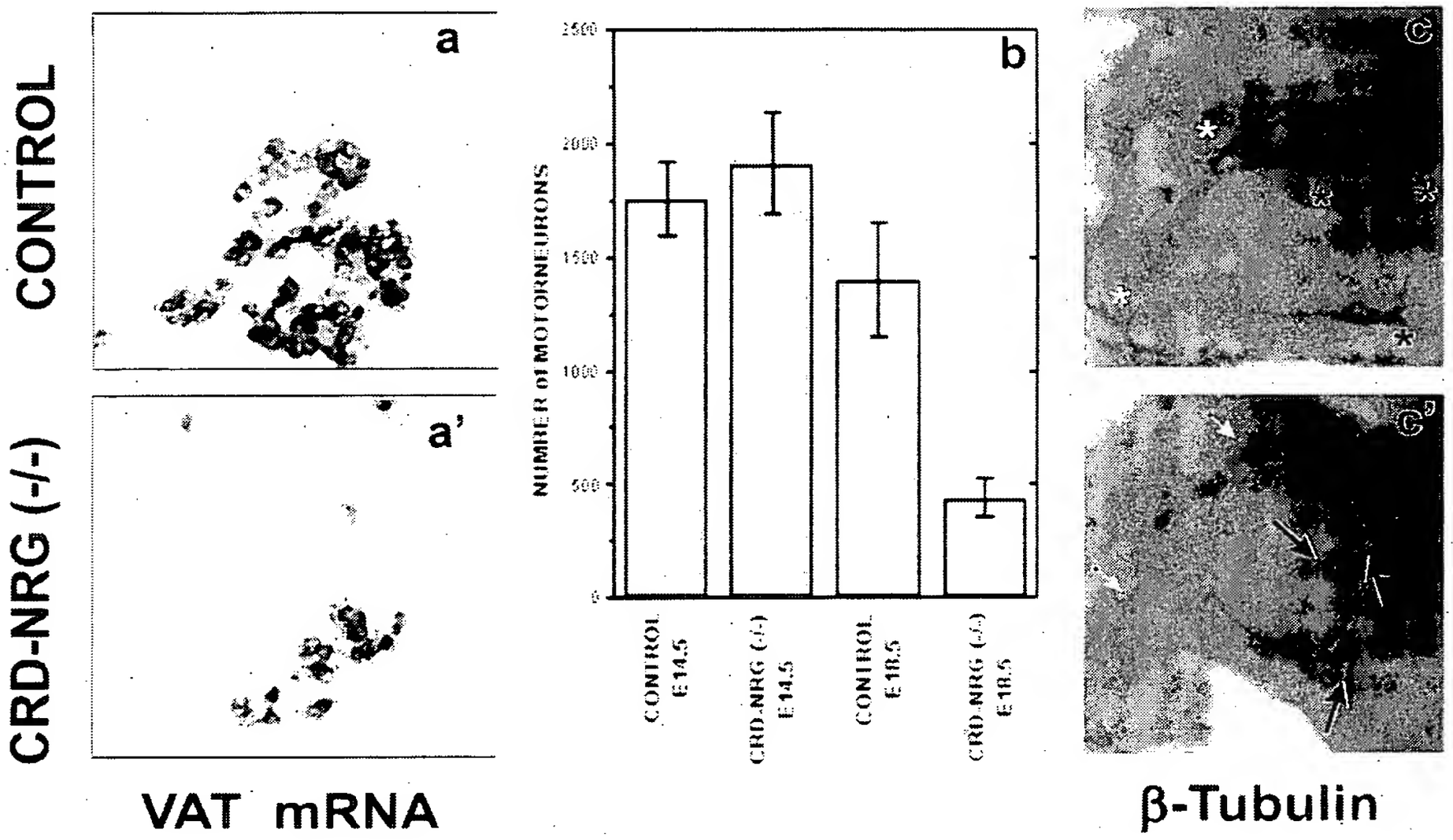
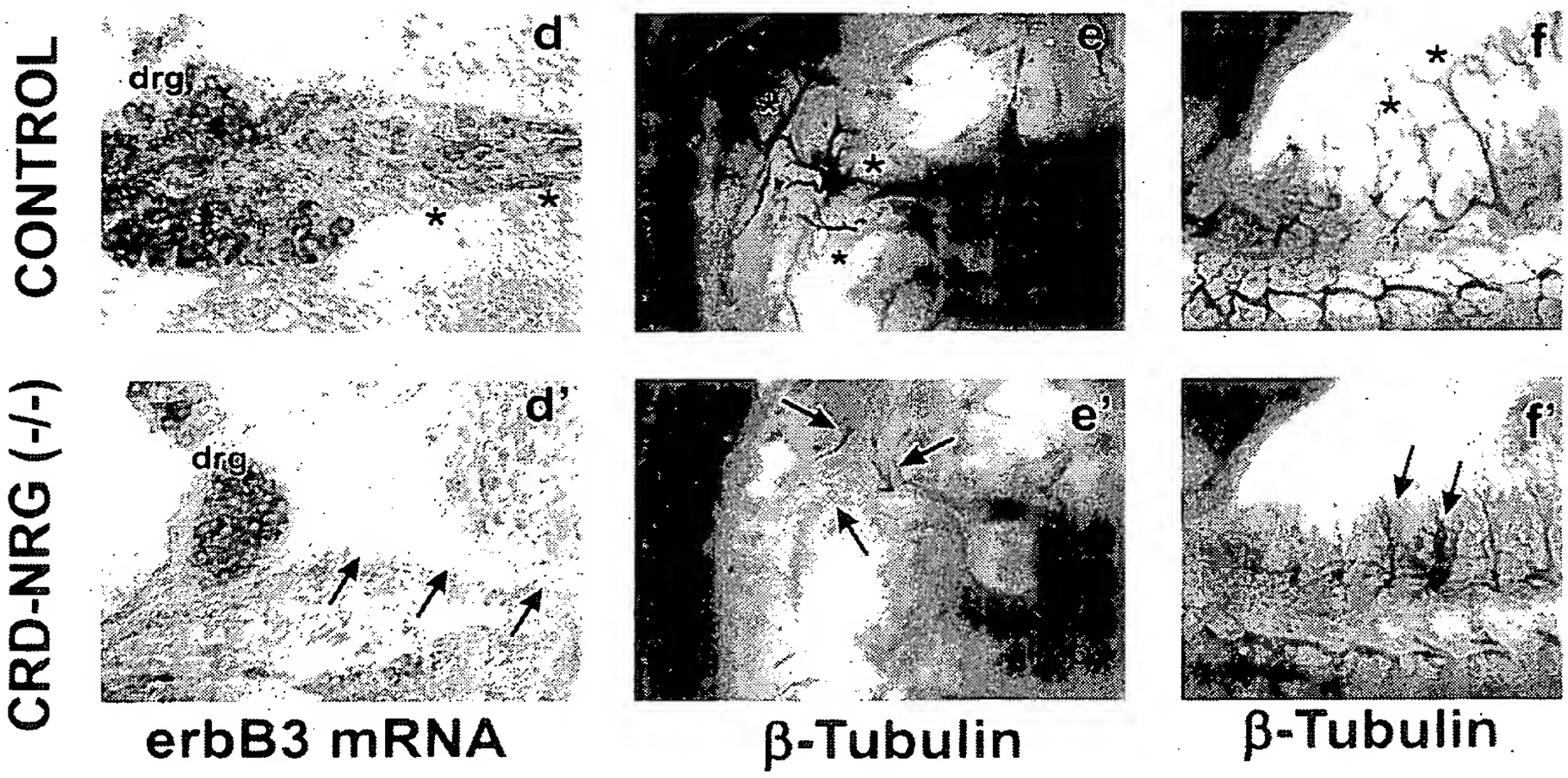


FIG. 22B



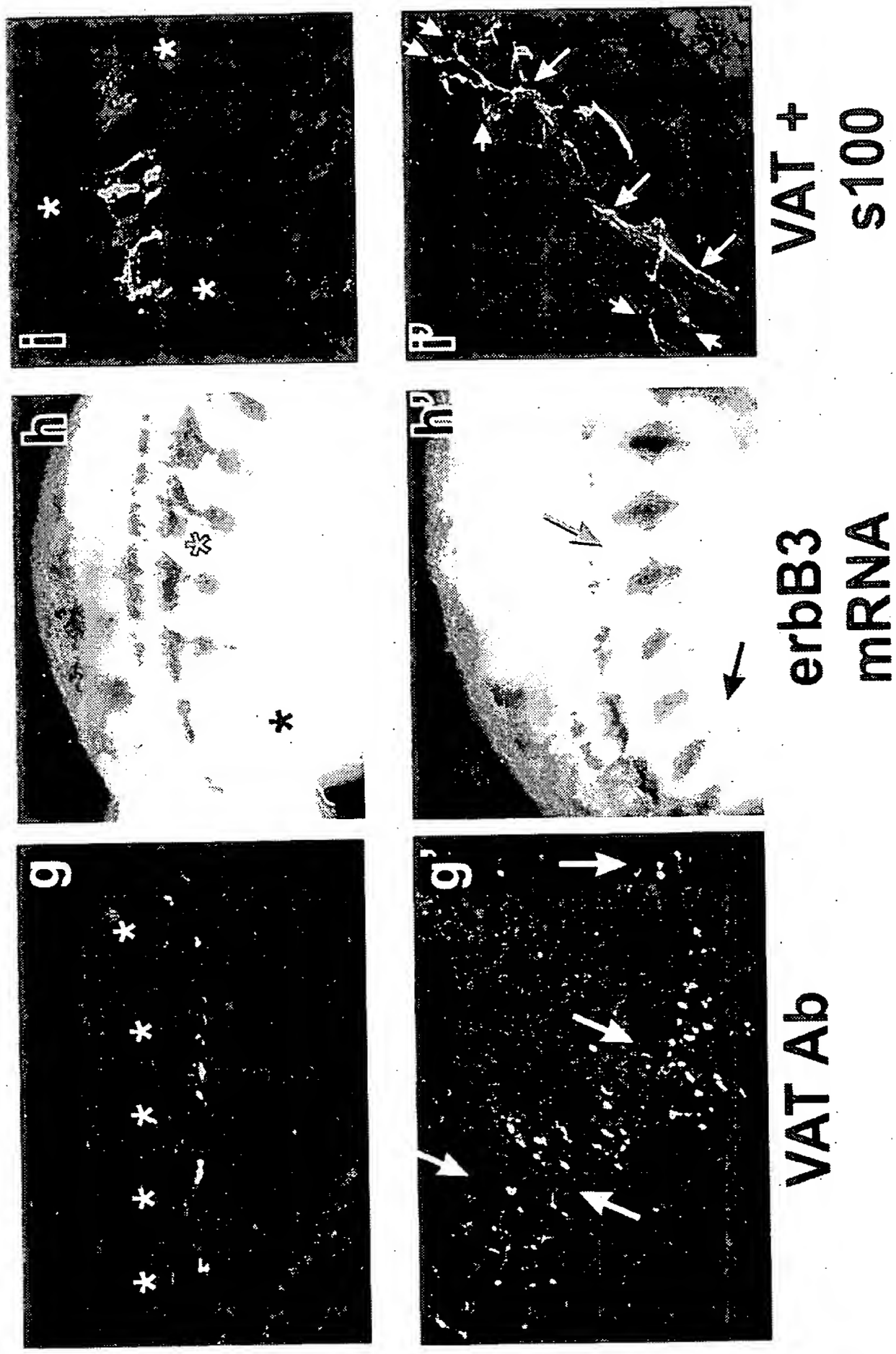


FIG. 22C

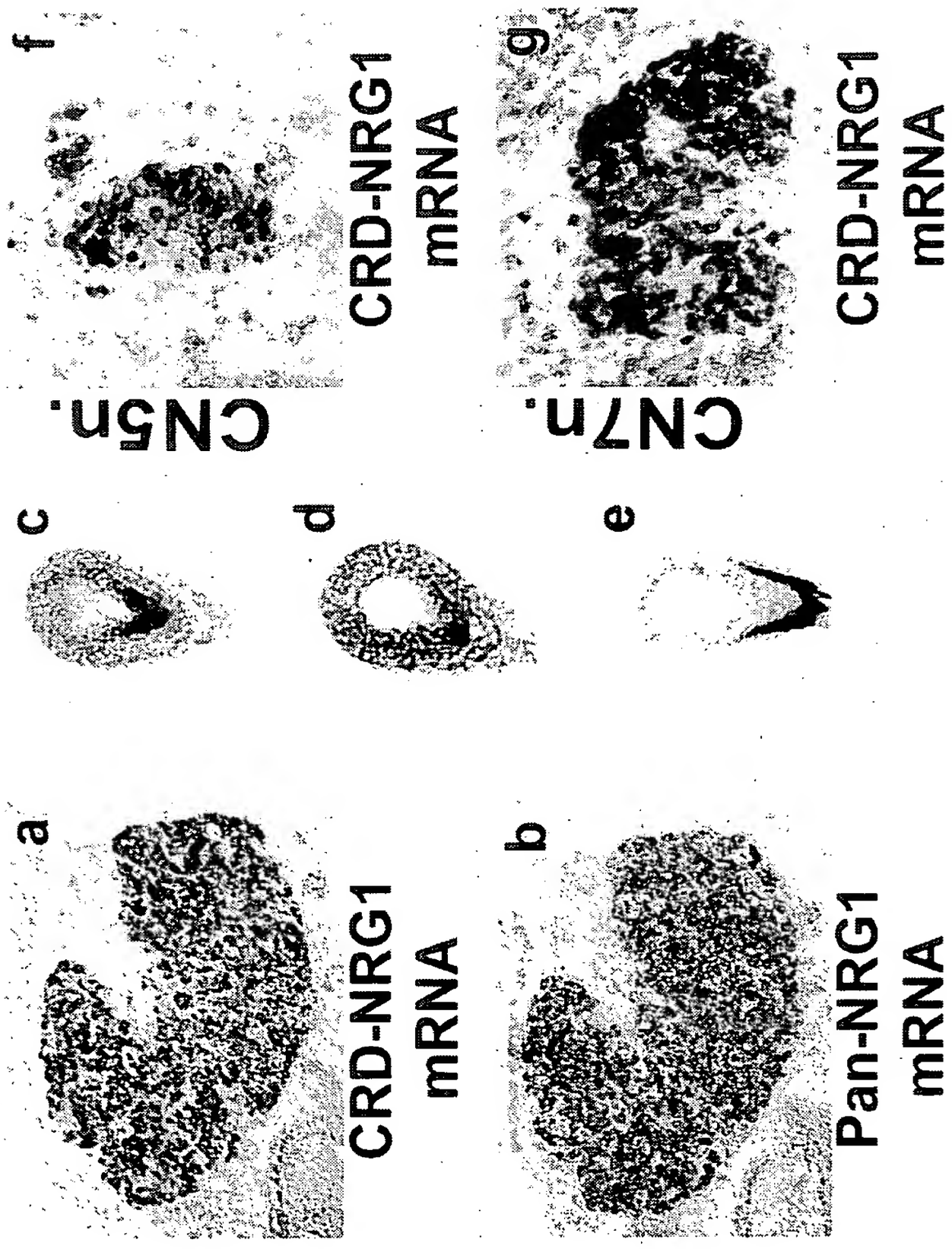
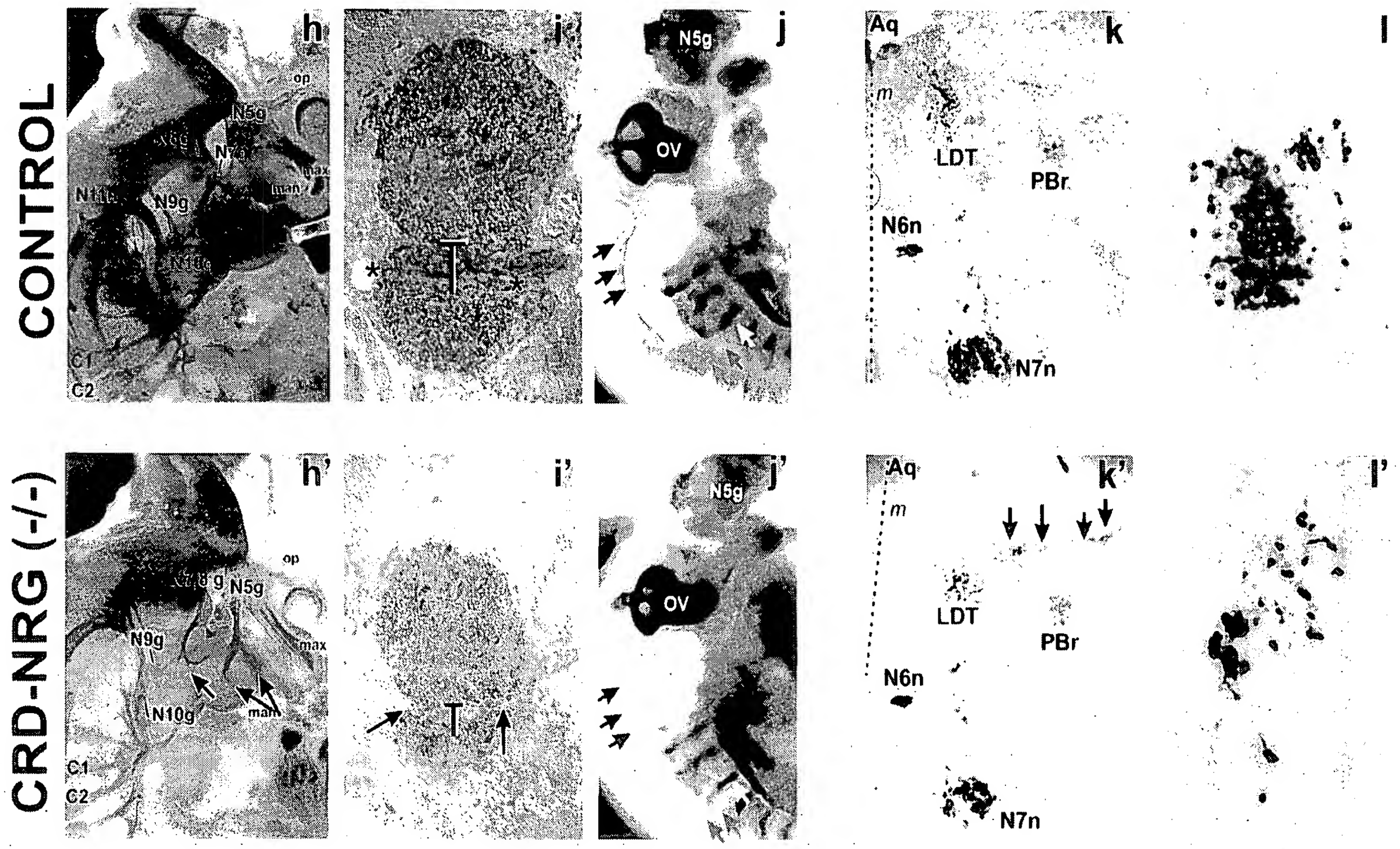

CN5-GANGLION
a
CRD-NRG1
mRNA
b
Pan-NRG1
mRNA
c
d
e
CN5n.
f
CRD-NRG1
mRNA
CN7n.
g
CRD-NRG1
mRNA

FIG. 23A

FIG. 23B



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